The Journal of Thoracic Surgery

VOL. 26 OCTOBER, 1953 NO. 4

Original Communications

BRONCHIOLAR ("ALVEOLAR CELL") CARCINOMA OF THE LUNG

CAPTAIN CLIFFORD F. STOREY, COMMANDER KENNETH P. KNUDTSON (BY INVITATION), MEDICAL CORPS, UNITED STATES NAVY, AND BENJAMIN J. LAWRENCE, M.D. (BY INVITATION)
ST. ALBANS, N. Y.

INTRODUCTION

BRONCHIOLAR or alveolar cell carcinomas constitute perhaps the least common,[1-6] the most interesting, and the most controversial group of primary pulmonary neoplasms. It has been held by a majority of observers that these tumors are of multicentric origin,[7-11] that they arise from the alveolar lining cells,[7, 10-13] that they are extremely rare, and that the prognosis of patients with this disease is unequivocally dismal.[2, 12, 14-17] If, indeed, these tumors invariably arise from multiple primary sites, no mode of treatment can be expected to be permanently beneficial and patients with this form of lung cancer must be judged as therapeutically hopeless.

Our interest in these lesions was stimulated when we encountered, within a relatively short period of time, three patients with small peripheral pulmonary nodules with essentially identical roentgen characteristics (Figs. 1, 2, and 3). Surgical treatment was promptly instituted in two of these cases, the lesion being removed by segmental resection in one patient and by excisional biopsy followed immediately by lobectomy in the other. Both of these patients are alive and well, one of them eighteen months and the other three and one-half years postoperatively. The third patient, whose lesion was demonstrated by serial chest roentgenograms to have remained stable for at least sixteen months, was subjected to an intensive diagnostic work-up, including multiple cultures of the sputum and gastric washings for acid-fast bacilli. While awaiting reports of the cultures, a spread was observed, first

From the Armed Forces Institute of Pathology, Washington, D. C., and the U. S. Naval Hospital, St. Albans, New York.

The opinions or assertions expressed herein are those of the authors and are not to be construed as official or reflecting the view of the Navy Department or the naval service at large.

Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

in the vicinity of the original lesion, but widespread dissemination soon occurred and all lobes of both lungs became involved with multiple, small, poorly circumscribed nodules (Fig. 4). A pericardial effusion developed and the bloody fluid obtained on pericardiocentesis contained malignant cells.

Fig. 1.

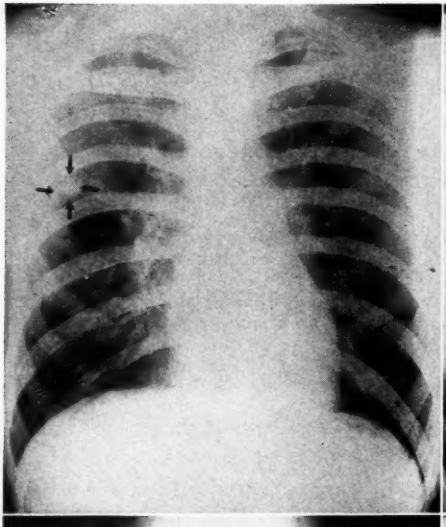
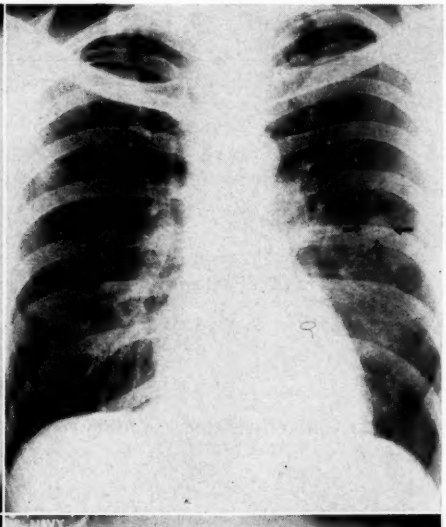


Fig. 2.



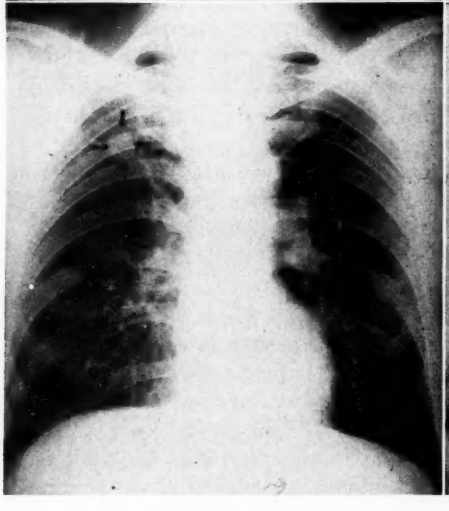


Fig. 3.

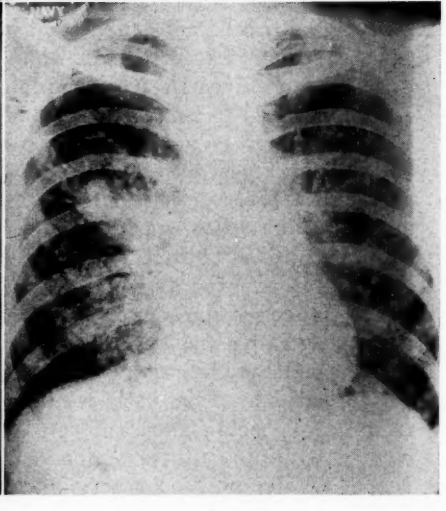


Fig. 4.

Figs. 1, 2, and 3—Chest roentgenograms of three pateints, each showing a small, circumscribed, peripheral, pulmonary nodule. Each patient has a bronchiolar carcinoma.

Fig. 4.—Chest x-ray view of the same patient shown in Fig. 1 made four months later. All lobes of both lungs are now involved by multiple, small, poorly circumscribed nodules. Bronchiolar carcinoma diagnosed by lung biopsy and verified at autopsy.

The diagnosis of bronchiolar carcinoma was established by lung biopsy. The patient died soon thereafter and complete post-mortem examination confirmed the diagnosis. There were widespread local and distant metastases.

The similarity of these three cases was striking and it seemed highly likely that metastases in the third case had taken place from a solitary primary lesion. The literature on this subject was reviewed and it failed to yield convincing evidence to support a number of commonly held opinions pertaining to these tumors. Particularly and most importantly, it has not been clearly shown that this neoplasm is of multicentric origin; on the contrary, there is a substantial array of data that would indicate that these carcinomas arise from a single primary lesion from which they spread to other sites as do most malignant tumors.[14, 18-21] In an attempt to clarify some of the moot points concerning this disorder, which has been termed "the mystery disease,"[22] a study of all available material concerning bronchiolar carcinoma was undertaken.

MATERIALS

The pathologic material at the Armed Forces Institute of Pathology, comprising a group of 39 clear-cut examples of bronchiolar carcinoma, was studied. Nine cases from the Institute have been previously reported by Swan[13] and one by Freedman.[23] Those cases are excluded from this report. Four personal cases and four collected from other sources have been added. Thus there has been provided a group of 37 hitherto unreported cases of this entity for review. Reports of 120 patients with this tumor have appeared in the literature since the publication of Swan's paper in 1949. He covered the literature through 1947. Swan[13] reported 9 cases and collected 27 which were not included in the review published by Neubuerger and Geever[17] in 1942. The latter authors had reviewed the literature up to 1942 and had collected 25 cases which they felt represented unmistakable gross and microscopic evidence of "alveolar cell tumor."

One hundred eight of the cases which we have collected from the literature have been abstracted and analyzed. Three cases reported by Drymalski, Thompson, and Sweany[30] and one reported by Graham and Delarue[40] were inadvertently misplaced and overlooked when the statistics were compiled and the graphs constructed. Three cases reported by Tillett and Hirsch[74] did not come to our attention until after the statistical studies had been completed. Five cases reported by Fisher and Holley[90] did not appear in the literature until after the graphs had been drawn. These twelve cases are therefore not included in the statistical studies. The 37 cases reported here have been added to the 108 collected cases to provide a group of 145 patients for statistical study. Where their data permitted, the 24 cases reviewed by Neubuerger and Geever,[17] the 27 collected by Swan,[13] and the 9 reported by him have been added to our material to make a total of 205 cases available for statistical analyses. One of the cases collected by Neubuerger and Geever, that of Fried, has been excluded because its authenticity has been

denied. To our knowledge, this includes essentially all unquestioned cases of this disease which have appeared in the literature from the first case report by Malassez[24] in 1876 to the present time.

NOMENCLATURE

In searching the literature for accounts of these tumors, one is impressed by the diversity of opinion regarding the benignancy or malignancy of the condition and its site of origin as well as by the conflicting claims of the proponents of sundry theories of etiology. No doubt this confusion has led different authors to select a variety of names by which to designate these neoplasms. Liebow[8] has compiled a list of thirty-six names by which these tumors have been called, and a considerable number which he did not include have been found in the literature. The sheer multiplicity of this nomenclature appears to reflect the lack of knowledge of the histogenesis of what appears almost certainly to be a single group of tumors. The term "bronchiolar carcinoma" has been adopted for the following reasons: 1. Carcinomas must, by definition, arise from epithelium; 2. an epithelial lining of the pulmonary alveoli has not been proved. On the contrary, there is a considerable weight of opinion, with which we concur, that the alveoli are not lined by epithelial but by mesenchymal cells; 3. bronchioles, on the other hand, are definitely lined by epithelium and therefore, from the histologic standpoint, certainly *could* serve as the site of origin of these tumors; 4. our own histologic studies, as well as those of numerous others, led us to conclude that the bronchioles are, in fact, their starting point.

The importance of the controversy which has raged as to the alveolar versus the bronchiolar origin of this group of neoplasms has been lessened, if not completely obviated, by the observations of Oppenheimer,[25] who feels that the doctrine of absolute specificity of the germ layers must be abandoned. She quotes Brachet[26] as stating, "In reality the germ layers like the blastomeres have an actual potentiality and a total potentiality; the former is what they normally become, the latter is what they are capable of forming, in addition, under diverse natural or experimental influences." Liebow[8] has pointed out that the distinction between the alveoli and the bronchioles as the site of origin may be somewhat fatuous as shown by Waddell's[27] observations which suggest that the epithelium lining the bronchioles may itself be of mesodermal origin. The important fact from the clinical standpoint is that these lesions arise *peripherally*. Whether from the alveoli or the bronchioles is largely a matter of academic interest.

There is strong evidence that the term pulmonary adenomatosis, implying as it does a benign lesion, is likely to be misleading and we feel that its use should be abandoned. Those who continue to employ that terminology acknowledge that metastases are seen in a significant percentage of cases,[28-30] even in those patients whose tumors appear histologically benign. Furthermore, not infrequently histologically benign and malignant areas are found in different portions of the same specimen, as in the cases reported by Dacie and Hoyle,[3] Wood and Pierson,[31] Laipply and Fisher,[32] and others.[16, 30, 33]

Serial sections in such cases have shown imperceptible merging of one into the other in some instances, and abrupt changes from benign to malignant in others. Whatever the diagnostic title selected, it would appear most desirable that common agreement be reached on an acceptable name for this group of tumors. Such an agreement would facilitate statistical reporting and would make more readily accessible reports in the literature pertaining to these lesions. Liebow[8] has adopted the term bronchiolar carcinoma and this nomenclature is also favored by Stewart.[34]

Swan[13] prefers that the term "pulmonary adenomatosis" be reserved for tumors which fulfill the following criteria: (1) alveolar-cell proliferation, characterized by the appearance of tall mucus-producing cells; (2) absence of an intrinsic tumor of the bronchial tree; and (3) absence of primary adenocarcinoma of any other part of the body. For those tumors which metastasize in addition, he coined the term "cancerous adenomatosis." Obviously this classification did nothing to lessen the confusion which already existed. Furthermore, Swan's diagnostic criteria would appear to be in need of revision. It is interesting to note, as a matter of fact, that in three of the cases reported by Swan[13] the criteria which he himself proposed were not fulfilled. Those three patients were not autopsied and one cannot be certain, therefore, that they did not have adenocarcinoma elsewhere in the body.

At the time when the diagnosis of this neoplasm was made almost exclusively at autopsy, the criteria proposed by Swan may have been practicable. Today, however, the diagnosis is often made by cytologic examination of the sputum or histologic study of the resected specimen. In addition the fact that these tumors are formed by *alveolar-cell* proliferation is far from proved. There is strong evidence to indicate, on the contrary, that the lesions have their inception in the basal cells of the terminal bronchioles. Although usually composed of tall columnar cells, they may be low columnar, or even cuboidal in type. Finally, mucus production is not an essential feature of this neoplasm. Many unequivocal examples of this tumor have produced little or no mucus. The following diagnostic criteria would appear more applicable to the lesions under discussion: (1) a tumor characterized by alveoli lined by epithelial cells of columnar or cuboidal type with eosinophilic cytoplasm and basally placed nuclei; (2) preservation of the pulmonary architecture; (3) absence of an intrinsic tumor of a bronchus; and (4) absence of *evidence* of primary adenocarcinoma in any other part of the body.

HISTOGENESIS

Passler, according to Fried,[35] was the first to give a comprehensive discussion of the origin of the cancer cells in bronchiolar carcinoma. In 1896 he reviewed 54 cases of lung cancer, of which he concluded 47 originated in the bronchial mucosa, while in the others the histogenesis could not be established. In 1912 Alder[36] published his monograph in which he reviewed 374 cases of carcinoma of the lung. He stated, "It is now held that carcinoma starting from the pulmonary alveoli is exceedingly rare, and some go as far as to deny its existence altogether."

Bell,[37] Ham and Baldwin,[38] Ikeda,[11] Sims,[33] Macklin,[39] and others believe that the epithelium in the fetus undergoes desquamation before the sixth month but that an occasional cell is left attached to the septal wall, proliferating in times of stress or strain on the alveolar epithelium. These authors were of the opinion that these septal cells, epithelial in nature, give rise to alveolar-cell tumors. The evidence in favor of an epithelial lining of the pulmonary alveoli has been ably summarized by Delarue and Graham,[40] who concluded that such a lining does exist and that "alveolar-cell carcinoma" probably takes its origin there. Herbut,[18] Smith and Gault,[41] Simon,[42] Sweany,[43] Bliss,[44] and Casilli and White[45] do not accept the alveolar origin of these tumors but rather believe them to arise from the lining of the terminal bronchioles. They base their opinion on the following premises: 1. There is no epithelial lining of the alveoli. 2. These tumors can be seen extending from bronchioles to alveoli, and 3. Histologically, the cells resemble the lining cells of the normal bronchiole.

Herbut[18] states that primary carcinoma of the lung arises from the basal cells of bronchi or bronchioles and further differentiation or lack of differentiation determines the distribution of these cells in relation to the rest of the pulmonary parenchyma. If the tumor forms cuboidal or columnar cells, they will line the alveolar septa in accordance with their inherent property to line spaces and so will produce the well-known alveolar distribution.

Our studies have shown no evidence of multicentric origin of the tumor within the lung. We believe the overwhelming evidence favors the unicentric origin from the lining of the terminal bronchioles with spread to other portions of the lung by way of the air passages following slough of the tumor cells, as well as by way of the lymphatics and the blood stream. Multiple primary cancers can and do occur, of course, particularly in paired organs.[40] The burden of proof, however, lies with the one who contends that multiple lesions of an identical histologic type represent primary tumors rather than metastases from a single source of origin. Dr. Evarts Graham[40] is one of many who is firmly convinced that this tumor is of multicentric origin, and he and Delarue have set forth clearly the evidence on which that conviction is based.

ETIOLOGY

There is a striking morphologic resemblance of bronchiolar carcinoma in man to jaagsiekte, an infectious disease in sheep. Jaagsiekte, a South African word derived from the Dutch, is the name given pulmonary adenomatosis when seen in sheep. The name means "driving sickness," and the symptoms appear in sheep when they are driven some distance. A virus etiology is strongly suspected since the disease is easily transmitted by housing infected sheep together with healthy sheep. Experimental transmission of the disease has been generally unsuccessful. Shepherds do not acquire the disease; however, several possible exceptions have been recorded. Histologically, the

lesions seen in jaagsiekte are composed of alveoli lined by a regular layer of nonciliated, high cuboidal epithelium, often papillary in nature, with prominent interstitial fibrosis. The stroma is seldom invaded. Aynaud and his associates[46] reported a case of jaagsiekte in sheep in which metastasis to mediastinal and hilar nodes occurred. These findings were later confirmed by Dungal and his co-workers.[47] There is no evidence to indicate that bronchiolar carcinoma in man is an infectious disease. Efforts to transmit the disease from man to laboratory animals have been unsuccessful. No causal relationship between the infectious disease in sheep and the malignant process in man has been shown, although a few reported cases of human bronchiolar carcinoma have been exposed to sheep ill with a pulmonary disorder.

Campbell[48] observed primary pulmonary tumors in mice when they were exposed to dust and tars of various kinds. He believed the tumors originated from alveolar cells which were originally benign and became malignant following continued irritation. The carcinogenic effects of urethane, dibenzanthracene, and other carcinogens in laboratory animals have been generally accepted. When these carcinogens are given subcutaneously, intraperitoneally, or intratracheally in susceptible mice, 100 per cent develop multiple lung tumors within four months. The histologic structure of these induced tumors is similar to the bronchiolar carcinoma seen in man. Metastasis to hilar nodes has been described. Review of the reported cases and those in this series fail to suggest a close etiological relationship between any of the common irritants and bronchiolar carcinoma. The necessity for caution in the application of results obtained in laboratory animals to disease processes in human beings is well recognized.

PATHOLOGY

Gross.—(Fig. 5.) Bronchiolar carcinoma consistently begins in the peripheral portion of the lung. The tumor frequently presents as discrete nodules varying in size from several millimeters to ten centimeters in diameter. The nodules are usually irregular in outline with sharp borders demarcating them from the adjacent lung tissue. In some instances there is a coalescence of the nodular masses, giving a striking resemblance to the stage of gray hepatization of lobar pneumonia. On cut section, the surface varies from gray-tan to yellow-brown and is moderately firm in texture. Mucus often exudes from the sectioned tumor. Cavities within the tumor are rarely noted. Large gross areas of atelectasis are seldom seen but irregular focal areas of atelectasis adjacent to the tumor are frequently present.

A constant gross finding is the absence of primary involvement of the major bronchi. In rare instances where the tumor had grown to large size late in the course of the disease, the bronchi may be secondarily invaded by the surrounding tumor. Frequently, the nodules extend to the pleura where they appear as slightly raised, umbilicated masses. Pleural effusion is fairly common and is often serosanguineous in character.

Microscopic.—(Figs. 6 to 15.) The histologic structure of bronchiolar carcinoma is characteristic and distinct. The tumor is composed of alveoli lined

by cells which are usually tall but they may be of the low columnar or even cuboidal type. The cytoplasm is eosinophilic. The nuclei are located basally and are round or ovoid in shape. The cells are almost always nonciliated and are attached at their base to the unaltered alveolar wall. In at least three reported instances the lining cells have been ciliated. The architectural pattern of the lung is seldom interrupted, the tumor cells appearing to outline the lumina of the alveoli and terminal bronchioles. In general, the growth pattern is remarkable for its uniformity. Characteristically the tumor

Fig. 5.—Gross specimen of a lung showing the typical appearance of bronchiolar carcinoma. Multiple small subpleural nodules are well shown.

is made up of well-differentiated cells without anaplasia, but lesions with more malignant features are encountered and the histologic picture may vary in different portions of the same tumor. Mitotic figures are rare in the typical case. The tumor cells show papillary formation within the alveoli and frequently desquamate into the alveoli. Mucicarmine stains usually, but not invariably, reveal mucin present within the cytoplasm of the tumor cells as well as in the extracellular spaces. Vacuoles of variable size in the cytoplasm are proved to contain fat when differentially stained with Sudan III.

Fig. 6.

Fig. 7.

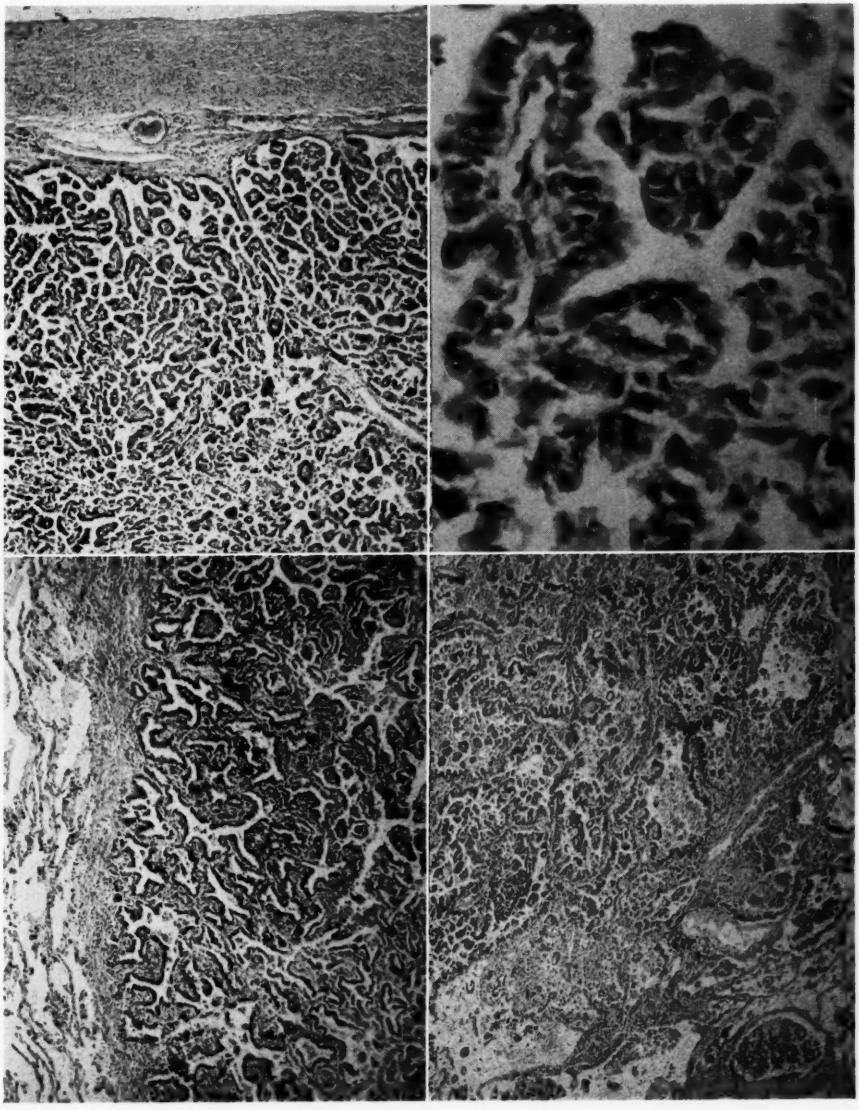


Fig. 8.

Fig 9.

Fig. 6.—Typical low-power view of bronchiolar carcinoma (×71).

Fig. 7.—High-power view showing alveoli lined by columnar neoplastic cells with a tendency to papillary formation (×594).

Fig. 8.—Jaagsiekte in lung of sheep (×71).

Fig. 9.—Bronchiolar carcinoma showing desquamation of tumor cells in alveolar spaces (×71).

Fig. 10.

Fig. 11.

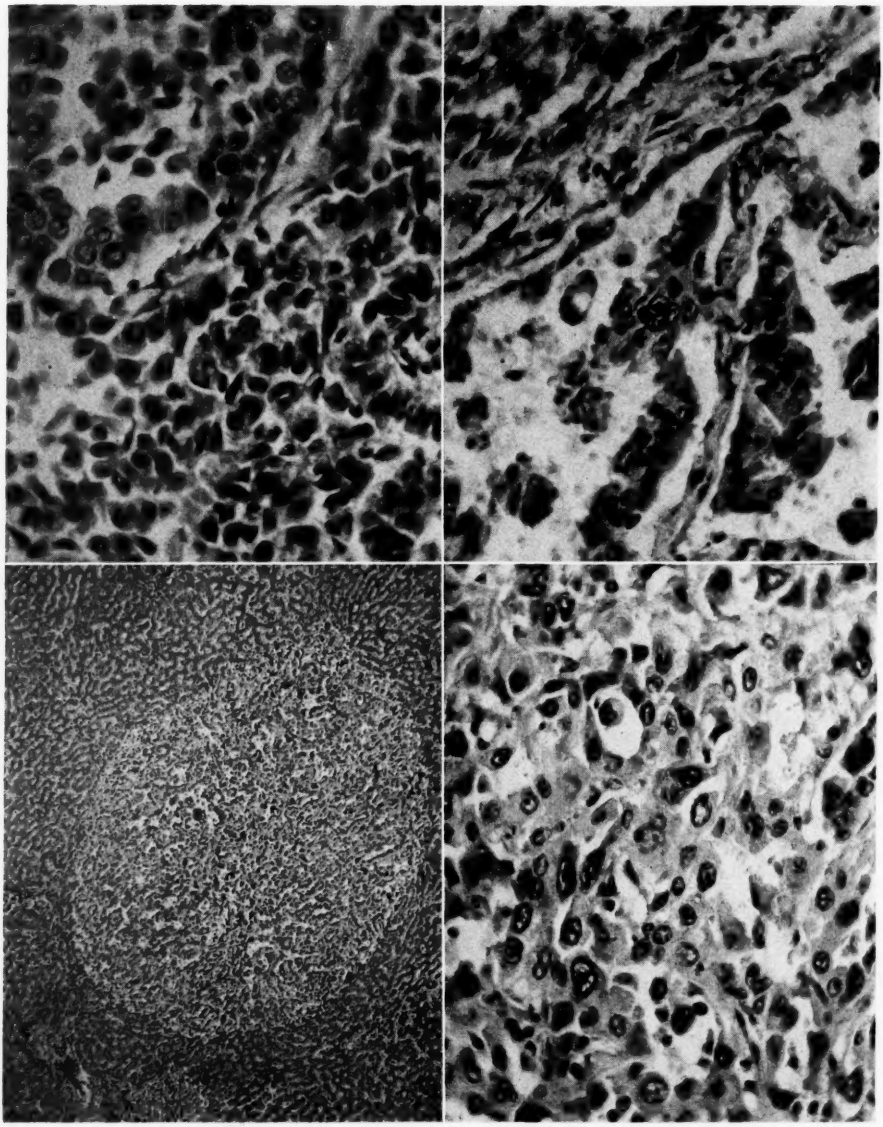


Fig. 12.

Fig. 13.

Fig. 10.—High-power view showing desquamated tumor cells (×570).
Fig. 11.—Section showing area of anaplasia with occasional signet ring cells (×570).
Fig. 12.—Focal area of metastasis in liver from bronchiolar carcinoma (×80).
Fig. 13.—Giant- and spindle-cell variant of bronchiolar carinoma (×570).

The stroma of the pulmonary septa may be normal or contain an increased number of thick collagen fibers. Elastic fibers are inconspicuous. Foci of inflammatory cells, the majority of which are polymorphonuclear neutrophils, are most commonly associated with foci of necrosis. Anthracotic pigment is occasionally phagocytized by the tumor cells. Psammoma bodies are infrequently found in sections of the tumor and, when present, are usually surrounded by tumor cells.

Fig. 14.

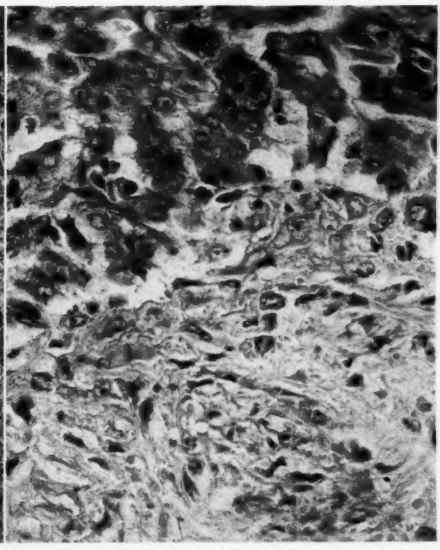


Fig. 15.

Fig. 14.—Bronchiolar carcinoma in which desmoplasia (upper left) is a prominent feature (×76).

Fig. 15.—High-power view of desmoplastic reaction adjacent to the tumor (×570).

Lymphatic invasion of the lung is demonstrable in sections from over 50 per cent of the cases. Small nests of tumor cells are conspicuous in the perivascular lymphatics. Clusters of tumor cells are frequently found lying free in the alveolar spaces in the tumor-bearing area as well as in distant portions of the bronchial tree. Intrapulmonic spread would be expected to occur when malignant cells are inspired into the air spaces and there set up new growths on the alveolar septa.

The review of cases in this series which had been diagnosed as pulmonary adenomatosis showed no significant changes in gross and microscopic findings from that seen in bronchiolar carcinoma. Examination of the hilar and mediastinal lymph nodes in cases of so-called pulmonary adenomatosis revealed the presence of metastatic tumor. In view of the evidence that this tumor does metastasize locally within the lung and to lymph nodes and other organs, the use of the term "pulmonary adenomatosis" no longer seems tenable, and the tumor should be classified as bronchiolar carcinoma.

CLINICAL FEATURES

Incidence.—It has been variously estimated that this tumor constitutes between 1½ and 5 per cent of all pulmonary carcinomas. It appears that the latter figure is more nearly correct.[10, 17, 30] In our experience the incidence has approximated 5 per cent. There is conclusive evidence to indicate that these tumors are frequently reported as peripheral adenocarcinoma, and it appears almost certain that this tumor is not as rare as it is reputed to be.

Racial Incidence.—A vast majority of the reported cases have occurred in the Caucasian race (Fig. 16). Among 205 patients, the race was given for 116, of whom 111 (95.7 per cent) were white. In view of the fact that a large percentage of the reported cases have been from this country, where Caucasians constitute approximately 90 per cent of the population, it appears that these tumors exhibit no racial predilection.

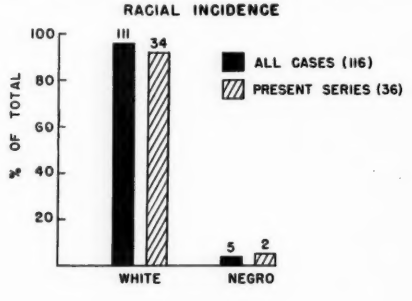


Fig. 16.

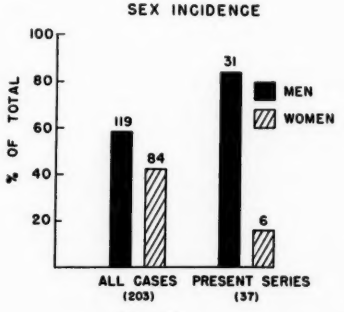


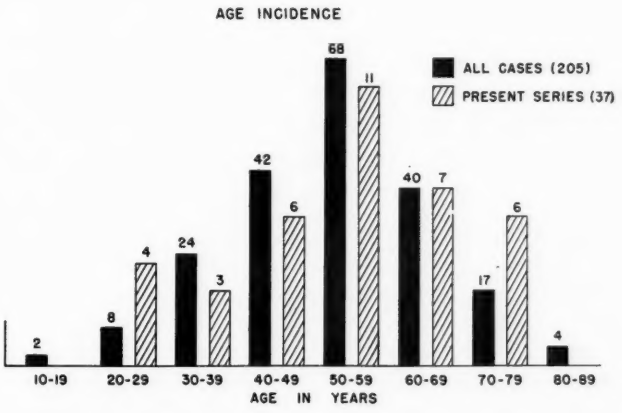
Fig. 17.

Figs. 16 and 17.—The number of patients on which these and the succeeding graph are based will vary from graph to graph. This is necessitated by the fact that reports of cases collected from the literature varied in their completeness and all of the desired data were not available on each of the cases.

Sex Incidence.—Many authors have observed that bronchiolar carcinoma occurs with approximate equal frequency in women and men.[2, 8, 11, 17, 30, 49] Among the 205 cases analyzed, the tumors were in men in 119 instances (58 per cent), in women 84 times (41 per cent); the sex was not indicated in the two case reports (1 per cent) (Fig. 17). These figures are in sharp contrast to those applicable to bronchiogenic carcinoma, where a strong predominance in male patients has been clearly established. Various reports have indicated that the ratio of male to female among patients with bronchial carcinoma is at least 5 to 1 and may be as high as 10 to 1. It is generally believed that at least 80 per cent of the cases of the common forms of lung cancer occur in men. If one were to exclude the 37 cases reported herein from those collected from the literature, the residual group of 166 patients would consist of 88 men and 78 women, an almost equal sex distribution. The 37 new cases included in the present report represent chiefly military personnel or veterans, thus comprising a selected group consisting principally of men. These figures firmly substantiate the belief that there is no real sex predominance in bronchiolar carcinoma.

Age Incidence.—The youngest patient reported with bronchiolar carcinoma was a boy of 16 and the oldest, a man of 89 years. The average age was 54 years and the median age also 54 years. Fifty-four per cent of the patients were between the ages of 40 and 60 years, and 85 per cent fell in the age group of 30 to 70 years (Fig. 18). These patients were therefore predominately in the so-called "cancer age" and the age incidence of this neoplasm does not differ materially from that of bronchial carcinoma.

Fig. 18.



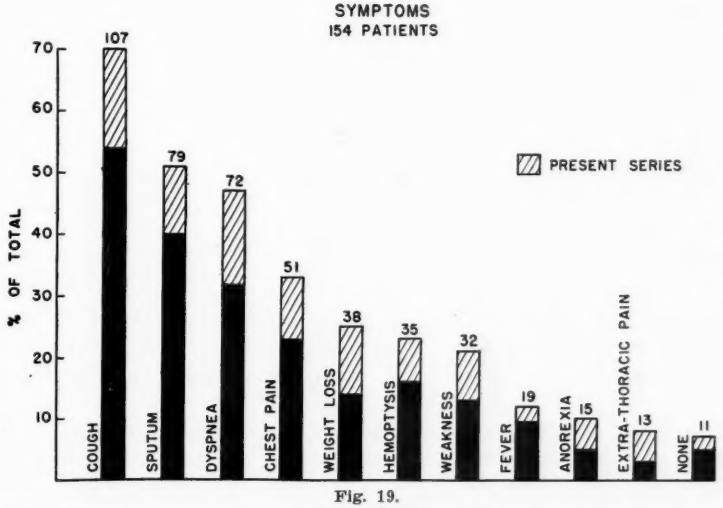


Fig. 19.

Fig. 19.—On this and several succeeding graphs the cases in the present series have been added to the collected cases and are graphically represented as percentage of the total.

Symptoms.—The presenting symptoms are shown in Fig. 19. In view of the fact that the patient's symptoms were frequently described incompletely,

if at all, in the original case reports collected from the literature, the figures on this graph must be interpreted as representing relative rather than absolute values. For example, cough, which is without question the most frequent symptom in patients with this tumor, was specifically mentioned in only 107 (70 per cent) of 154 patients. The percentage values in our group of 37 patients reflect more accurately the true incidence of the various symptoms. These data were obtained from the patient's original clinical records. The most common symptoms, in approximate order of frequency, are cough, sputum, dyspnea, chest pain, weight loss, hemoptysis, weakness, fever, anorexia, and pain other than in the chest.

It is noteworthy that 11 patients (7 per cent of 154 cases) had no symptoms. In these individuals the lesion was accidentally discovered on routine chest roentgenograms, and the diagnosis was made on histologic study of the excised tumor. There is reason to believe that the prognosis is much better in this group of patients than in those who sought medical care because of the presence of symptoms.

The character and degree of the cough in these patients was highly variable. In general it was not of the harassing type and was usually proportionate to the amount of sputum production. In a fairly large percentage of patients the cough was dry; in a majority of this group it was described as mild or slight.

The production of sputum, the second most common symptom, was encountered somewhat less frequently than cough. Numerous patients raised no sputum and the amount and character showed great variation among the patients whose cough was productive.

Dyspnea, a common symptom in the group as a whole, was not usually seen early in the course of the disease. The presence of dyspnea almost invariably indicated an advanced process with widespread pulmonary involvement. The degree of the dyspnea was most often directly proportional to the extent of the tumor, reflecting the degree of diminution of normally functioning lung tissue.

Chest pain, indicative of pleural involvement, was not an uncommon complaint. The pain was usually mild to moderate in character, rarely excruciating, and was definitely related to respiratory movements.

Weight loss, next in frequency, was also a late manifestation. It is, in fact, remarkable how few systemic symptoms these patients present until the disease process is far advanced. In general, weight loss was observed only after cough, expectoration, and dyspnea had become prominent. The majority of patients maintain an excellent nutritional status until they approach the terminal phase.

Hemoptysis is by no means as rare as some authors have considered it to be.[8, 16, 50, 51] It was rather often the first symptom, although the amount was usually small, often no more than streaking or pink-tinged sputum. Frank hemorrhages of serious degree rarely occur. Weakness, seen only in advanced disease, usually accompanies the onset of dyspnea and weight loss and like those symptoms does not make its appearance until there is massive pulmonary

involvement. Fever, although mentioned in 9 per cent of the cases, is not a characteristic feature. Many of these patients die of a terminal pneumonia and the presence of fever commonly denotes the presence of a suppurative or inflammatory pulmonary complication. Anorexia, a very late symptom, appears only when dyspnea has become marked. A majority of patients retain a satisfactory appetite until just before death. Extrathoracic pain, mentioned in 6 per cent of patients, although occasionally attributable to an unrelated cause, almost always denoted a distant metastasis. Cyanosis occurs only terminally.

A review of these symptoms makes clear their completely nonspecific character. Nothing in the symptomatology is characteristic of bronchiolar carcinoma; the symptoms are rather those of any extensive chronic pulmonary disease. This point is emphasized by the fact that the most common clinical diagnosis in these patients was pulmonary tuberculosis, followed (not necessarily in order of frequency) by such conditions as sarcoidosis, silicosis, bronchopneumonia, metastatic carcinoma, fungus disease, bronchiectasis, Hodgkin's disease, and atypical pneumonia.[12, 13, 24, 28, 32, 42, 49, 52]

Physical Signs.—There are also no physical signs that are characteristic or even highly suggestive of bronchiolar carcinoma. Those abnormal findings encountered will depend upon the location, character, extent, and distribution of the disease and upon the presence or absence of complications, such as pneumonia. The great variation of the physical findings from case to case makes it virtually impossible to tabulate the abnormal signs seen in patients with this neoplasm. Furthermore, no useful purpose would be served by recounting the findings on physical examination described in the individual case reports.

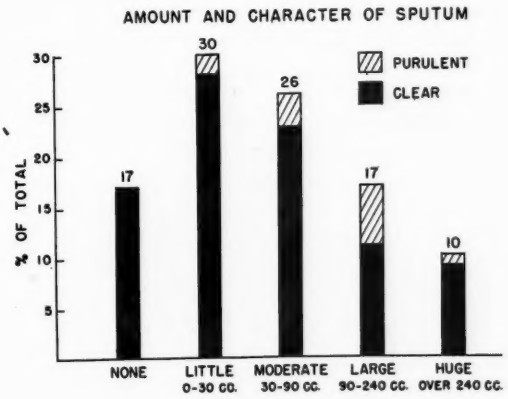


Fig. 20.

Amount and Character of Sputum.—Reference to the sputum was sufficiently precise to permit analysis in 100 patients. The results are shown in Fig. 20.

It has been emphasized repeatedly that this disease is characterized by the production of large amounts of clear, frothy sputum, but this point is scarcely borne out by the available data. Only 27 of 100 patients (27 per cent) raised more than an average of 90 c.c. in twenty-four hours. It is true that a number of patients produced fantastic quantities of sputum. For example, Fox[53] mentions a patient whose sputum production amounted to 3 to 4 quarts (2,839 to 3,785 c.c.) daily. Kennamer's[54] patient raised 3,122 c.c. (3.3 L.) in one twelve-hour period and usually brought up 2 to 3 pints per day. Kern, Lewinsky, and Curran[55] report a patient who, in less than four months, spat up 78.2 L. of expectorate (some 20 gallons of fluid), far exceeding his body weight of 67.1 kilograms. Sputum production reached nearly 2,000 c.c. in some twenty-four hour periods and often exceeded the urine output. The patient reported by Rey and Rubenstein[56] raised 1,500 c.c. daily, and Wood's[57] patient produced up to 1 quart (946 c.c.) a day.

It is obvious that, if long continued, a huge daily sputum output will result in serious fluid, electrolyte, and protein depletion. These outstanding examples of severe bronchorrhea are scarcely characteristic, however, of the typical patient with this tumor. Of the patients, 17 per cent had no sputum, and 56 per cent raised less than 90 c.c. daily. Thus the sputum production varied from none to moderate in quantity in 73 of 100 patients. The character of the sputum has been described as clear, watery, glairy, frothy, mucoid, or resembling pale soapsuds. This description of the typical sputum may be accepted as an accurate one, for it was of this type in 71 of 83 patients whose sputum was adequately described. Only 12 of 100 patients (12 per cent) raised mucopurulent or frankly purulent sputum and in a majority of these individuals complications, such as bronchiectasis or bronchopneumonia, were present. Only 1 of 100 patients had excessively large quantities of purulent sputum.

Hemoptysis.—A number of writers on the subject of bronchiolar carcinoma have stated that hemoptysis rarely occurs.[8, 16, 50, 51] Such is not the case. The patients in whom adequate data concerning the sputum were available have been analyzed as to the presence or absence of hemoptysis and the results are given in Fig. 21.*

It will be noted that blood-spitting occurred on one or more occasions in 35 of 71 patients (49 per cent) in whom hemoptysis was specifically mentioned as to its presence or absence. Since blood was definitely raised by 35 of 100 patients whose sputum was described at all, it occurs in at least 35 per cent of patients with this malignancy. Furthermore, it scarcely can be assumed that none of the 29 patients in whom hemoptysis was not directly mentioned never spat blood during their illness. Hemoptyses were usually small but often occurred repeatedly. This symptom is not necessarily a late one. In a number of reported cases as well as in several patients in this series, hemoptysis was one of the earlier complaints.[9, 10, 13, 14, 17, 20, 29, 54, 58-62]

Duration of Symptoms.—The prevailing opinion appears to be that bronchiolar carcinoma is a slowly progressive chronic pulmonary new-growth which

*Watson and Smith did not describe the sputum in their patients and those cases are not included in this graph. They mentioned hemoptysis in 9 of their 33 pateints, however.

is not a debilitating disease until very late, that it gives rise to remarkably few systemic symptoms, and usually kills by the sheer extent of the pulmonary involvement.[6, 42, 50, 51, 63] This impression of its chronicity is well substantiated by the reported figures. The clinical data permitted analysis of 151 patients in respect to the duration of symptoms. The results are shown in Fig. 22.

The duration has been calculated from the time of onset of symptoms clearly attributable to the disease to the date of death if the patient died, to the date of operation if resection was carried out and the patient has remained free of symptoms postoperatively, and to the date of the last report of patients with recurrent or persistent symptoms with or without surgery.

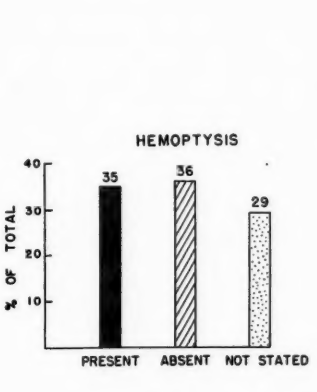


Fig. 21.

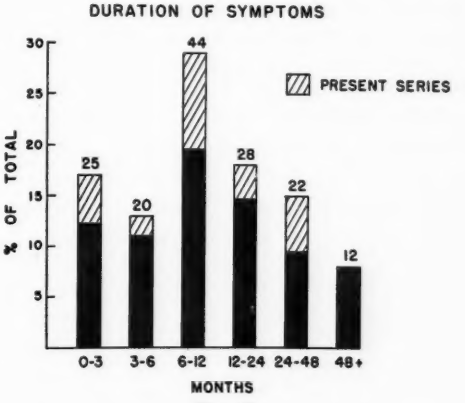


Fig. 22.

It is entirely possible that the criteria have been too rigid in evaluation of the patient's symptoms and the average duration of symptoms may be longer than the figures in the above graph would indicate. In a number of reported cases as well as several of our own, symptoms suggestive of a pulmonary disorder were present considerably longer than we have indicated. It has been deemed advisable, however, to date the duration from the time of the appearance of symptoms which without reasonable doubt can be ascribed to the neoplasm. On that basis, symptoms were present less than six months in only 30 per cent of the patients. Their duration exceeded one year in 41 per cent and two years or more in 34 patients or 23 per cent of the group analyzed from this standpoint. The 45 patients whose symptoms were of relatively short duration includes those who never had symptoms as well as many of those who received the benefits of early excisional surgery.

ROENTGENOGRAPHIC FINDINGS

Valentine and Wynn-Williams,[29] in summarizing the clinical and radiologic features of three cases which they reported, stated that "the clinical and radiological appearance of these three patients are typical of those hitherto described in that they are unalike, suggestive only in their variability and

undiagnosed before death." Their statement adequately summarizes our own impression of the roentgenographic findings in patients with bronchiolar carcinoma.

One hundred fifty-three cases, including those reported here, have been collected in which the chest roentgenograms were illustrated, available for review, or in which the x-ray findings were described in sufficient detail to permit their classification. To diagram them all accurately would require an impractical number of drawings. It has been possible, however, to devise twelve diagrammatic figures which depict with reasonable accuracy the radiographic picture presented by these lesions. The diagrams are shown in Fig. 23.

Bilateral nodular lesions, varying in size from a millet seed to a cherry, rounded in contour but with indistinct margins fading imperceptibly into the surrounding lung and involving all lobes of both lungs, often have been said to be characteristic of this variety of lung cancer. Fortunately, this hopeless picture is encountered in but 20 per cent of patients at the time of the first chest x-ray film which demonstrates their lesion. The fact that these tumors are first observed as a solitary peripheral nodule in 26 per cent of the patients provides ample reason from considerable optimism. More than two-thirds of the patients showed unilateral lesions on their first radiographic examination.

In slightly over one-half of the entire group the tumors were apparently confined to one lobe at the time of their discovery. A pleural effusion was present on the occasion of the initial examination in 8 per cent of the patients and this often obscured the primary pulmonary lesion. It must be borne in mind that these illustrations are purely diagrammatic; in actuality, the sharp distinction between the diffuse consolidated type of disease and that presenting as multiple nodules, as depicted, is distinctly uncommon. Far more frequently, areas representing each of these types are simultaneously present and they fade into one another. Sufficient coalescence of multiple nodules gives rise to a homogeneous density. A complicating pneumonia will produce the same picture. Although classic examples of the diffuse and nodular types are occasionally encountered, they are the exception rather than the rule and represent but a stage in the disease process. Separation of the lesions in these patients into the two types seems to be a purely artificial division, dependent almost solely upon factors such as the stage at which the patient is observed and the presence or absence of complications. In this connection it is interesting to note that in the case described by Malassez,[24] the first example of this entity to be reported and the prototype of the nodular form of the disease, there was present, in addition to multiple nodules, diffuse consolidated areas. Furthermore, Musser's[64] case, the first patient with the diffuse form to be reported, presented multiple nodules as well as diffuse consolidation.

Nodular lesions eventually coalesce in patients who survive sufficiently long to permit this to occur. Serial films frequently demonstrate marked changes in the radiographic picture. It can be concluded, therefore, that

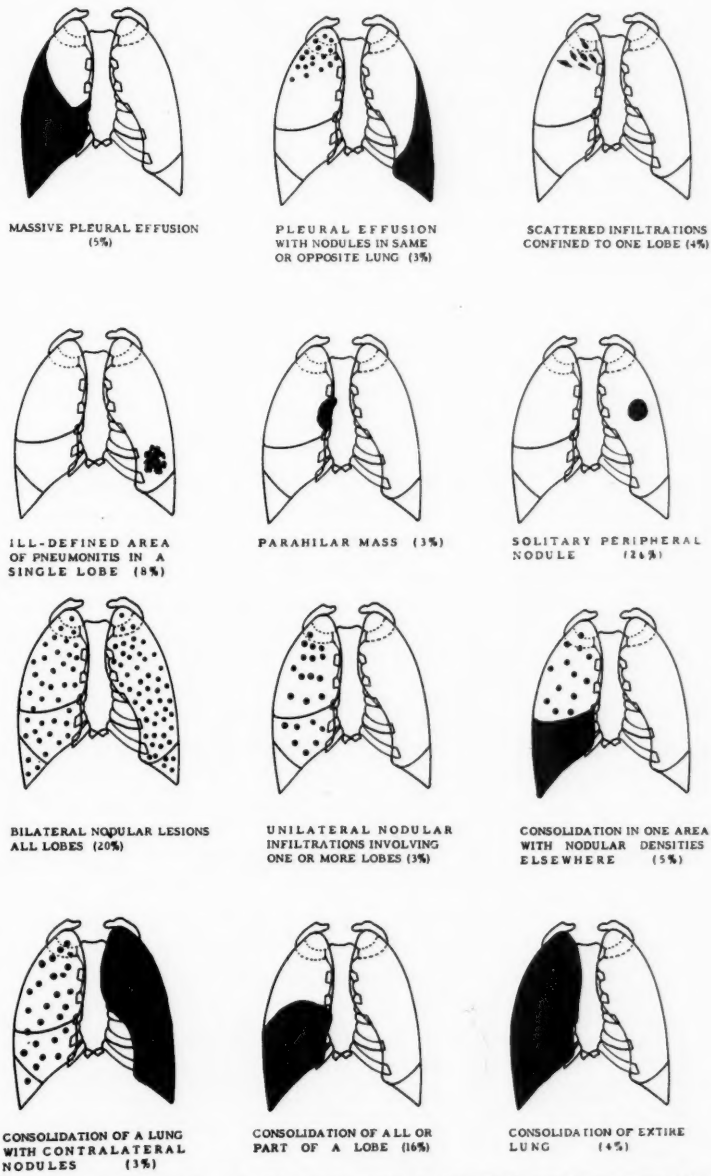

MASSIVE PLEURAL EFFUSION (5%)
PLEURAL EFFUSION WITH NODULES IN SAME OR OPPOSITE LUNG (3%)
SCATTERED INFILTRATIONS CONFINED TO ONE LOBE (4%)
ILL-DEFINED AREA OF PNEUMONITIS IN A SINGLE LOBE (8%)
PARAHILAR MASS (3%)
SOLITARY PERIPHERAL NODULE (2.6%)
BILATERAL NODULAR LESIONS ALL LOBES (20%)
UNILATERAL NODULAR INFILTRATIONS INVOLVING ONE OR MORE LOBES (3%)
CONSOLIDATION IN ONE AREA WITH NODULAR DENSITIES ELSEWHERE (5%)
CONSOLIDATION OF A LUNG WITH CONTRALATERAL NODULES (3%)
CONSOLIDATION OF ALL OR PART OF A LOBE (16%)
CONSOLIDATION OF ENTIRE LUNG (4%)

Fig. 23.—Diagrammatic outline of the lesions seen in the chest roentgenograms of patients with bronchiolar carcinoma at the time of their first radiographic examination.

there is no characteristic x-ray appearance of bronchiolar carcinoma. The disorder may mimic almost any variety of pulmonary lesion; a small number of patients have even shown cavitation on x-ray examination. It is an unfortunate fact that those patients exhibiting the most suggestive picture are those with far-advanced bilateral lesions. In this situation the diagnosis is a matter of interest but not of importance, for the prognosis in such patients is utterly hopeless.

METHOD OF DIAGNOSIS

Although this tumor was first described by Malassez[24] seventy-seven years ago, until fairly recently the diagnosis was made only at post-mortem. The diagnosis of this neoplasm was first made in a living patient in 1936 when Skorpil[60] did a left upper lobectomy for a lesion which proved to be a bronchiolar carcinoma ("alveolar epithelial carcinoma'). No further cases were diagnosed ante mortem until the resection by Wood and Pierson in February, 1943. They removed the left lower lobe for a pulmonary lesion of uncertain type. Histologic examination showed it to be a bronchiolar carcinoma. Graham[40] performed lobectomy in June, 1943, for a similar lesion, the third patient with this neoplasm to be treated surgically. Among the cases which we have reviewed, the method of diagnosis was clearly stated in 146 instances. The diagnostic methods are shown in Fig. 24.

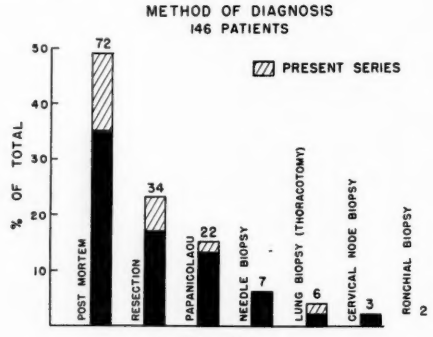


Fig. 24.

The increasing efficiency of the diagnostic methods now employed in patients with this malignancy is evidenced by the fact that although only one patient was diagnosed ante mortem prior to 1943, since that time at least 75 patients of record have been correctly diagnosed during life. The recent more frequent utilization of early excisional surgery in the management of patients with solitary peripheral nodules or persistent pulmonary infiltrates of uncertain etiology has resulted in a sharp increase in the number of patients diagnosed prior to death. Thirty-six patients with bronchiolar carcinoma have been diagnosed by histologic examination of the resected specimen.

By far the most promising of the newer diagnostic methods is cytologic examination of the sputum by the Papanicolaou technique. The first patient with this disease in whom the diagnosis of pulmonary malignancy was estab-

lished by this means was reported by Acevedo, Giuntini, and Croxatto[65] in 1944. The diagnosis was made in 1942 and was subsequently confirmed at autopsy. Hatfield and Hill[66] reported a patient with bronchiolar carcinoma in 1949 in whom the Papanicolaou stain was positive for malignant cells and again the post-mortem findings were confirmatory. In the same year Smith, Knudston, and Watson[67] reported 4 patients with bronchiolar carcinoma in whom the Papanicolaou was Class V. Two of those patients were diagnosed in 1947 and two in 1948. Since that time, 16 additional patients, including 3 reported here, with proved bronchiolar carcinoma have been accurately diagnosed as having pulmonary malignancy by cytologic examination of the sputum.[10, 52, 58, 68-70] In other reported cases, the Papanicolaou has been strongly suggestive of cancer.[55, 58]

Papanicolaou[71] has noted that this tumor exfoliates profusely and yields abundant material characteristic of this type of neoplasm. Good and associates[10] and McDonald and Woolner[72] also feel that in certain instances cells in the sputum possess characteristics that will permit the examiner to suggest the diagnosis of bronchiolar carcinoma. The typical findings consist of clumps of columnar cells with a free border of cytoplasm and fairly regular nuclei. These are felt to consist of groups of cells representing papillary projections which have broken off and been expectorated. Fried[35] and others have commented upon the loose attachment of the abnormal cells lining the alveoli and the ease with which they become detached. In a case mentioned but not reported in detail by McCoy,[52] the specific diagnosis of bronchiolar carcinoma was suggested by Dr. Papanicolaou on the basis of the sputum findings and that diagnosis was verified following resection of the lesion. The value of this diagnostic method is further emphasized by the report of Watson and Smith.[58] The sputum of 15 patients who proved to have bronchiolar carcinoma was studied. In 9 the sputum was positive for malignancy and in 3 it was strongly suggestive of cancer. Thus in 80 per cent of this group the sputum was either definitely positive or highly suggestive of carcinoma. These findings emphasize the necessity of repeated careful cytologic examination of the sputum of patients suspected of having this disease.

Among the other diagnostic methods, needle or aspiration biopsy, lung biopsy at open thoracotomy, and peripheral lymph node biopsy have each established the diagnosis in a small percentage of cases. Aspiration biopsy would appear to be indicated only in far-advanced cases with extensive pulmonary consolidation. Thoracotomy and lung biopsy without further resection has been used in patients with widespread bilateral disease. Patients with lesions of this type are doomed if the biopsy shows bronchiolar carcinoma; the justification for its use lies in the hope that some condition will be found in which effective therapy can be instituted. Bronchial biopsy would not be expected to yield positive results in this disease which characteristically does not involve the larger bronchi. However, in patients in whom the disease process is far advanced, the bronchi may be secondarily involved and a chance biopsy may show histologic evidence of the tumor. Such was the case in the 3 reported patients in which a positive bronchial biopsy was obtained.[10, 58]

DISTRIBUTION OF DISEASE

When the information was available, the distribution of the disease within the lungs was determined on the basis of the interpretation of the patient's first chest roentgenograms showing the lesion. These data were correlated with the operative findings in those patients who were treated surgically. In the remainder, the distribution was determined on the basis of post-mortem examination. The results are shown in Fig. 25.

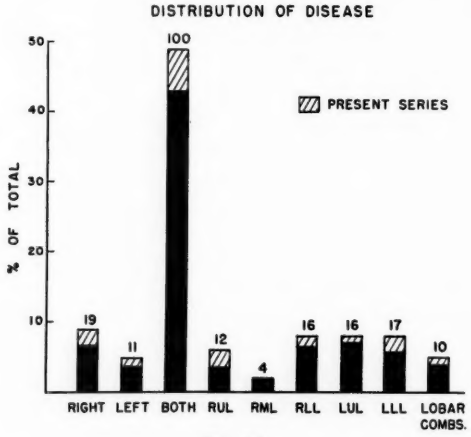


Fig. 25.

It will be noted that approximately 50 per cent of the patients had bilateral disease at the time that its extent was determined. However, these figures are weighted by the fact that information concerning the patient's chest x-ray films was not available in many cases (there were 52 such instances among the 205 patients). Under those circumstances the location of the lesions was determined at autopsy. When the involvement was unilateral the right and left lungs were affected with approximately equal frequency (51 and 44 times, respectively). There was no significant difference in the frequency of involvement of the various lobes. The figures on this graph do not agree with the distribution of this neoplasm as determined radiographically (Fig. 23). However, this graph is based on a larger series of patients, including many of the earlier cases in whom the diagnosis was established exclusively at autopsy.

METASTASES

The records of 168 reported patients and of the 37 patients in the present series, a total of 205, were reviewed from the standpoint of metastases. A summary of the findings is given in Figs. 26, 27, and 28.

Neubuerger and Geever[17] have stated that metastases occur in approximately 50 per cent of patients and that in about one-half of those showing metastases, the secondary deposits will be confined to the mediastinal nodes.

Their estimate of the incidence of metastases is confirmed by our findings. One hundred ten (54 per cent) of the cases reviewed showed metastatic lesions. In 38 patients (35 per cent of those with metastases) there was local spread only, and 40 patients (36 per cent of the metastatic group) showed both local and distant spread. Thus 71 per cent of those with metastases, or 38 per cent of the entire group of 205 patients, had involvement of the intrathoracic lymph nodes. An extremely interesting and important observation is that 32 patients, 29 per cent of those with metastases, or 15.6 per cent of the entire group, showed *distant spread only*. This demonstrates the frequency of blood-borne metastases.

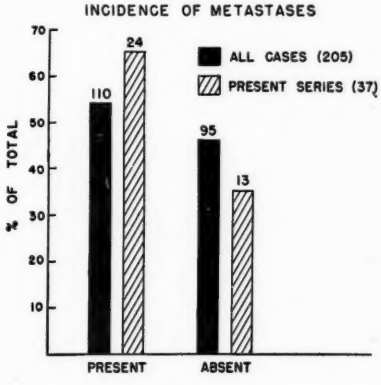


Fig. 26.

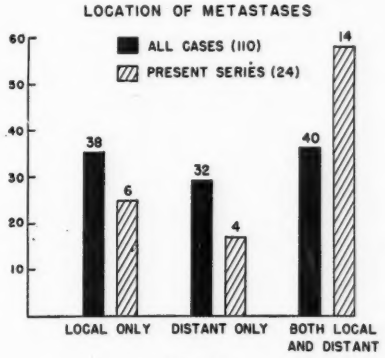


Fig. 27.

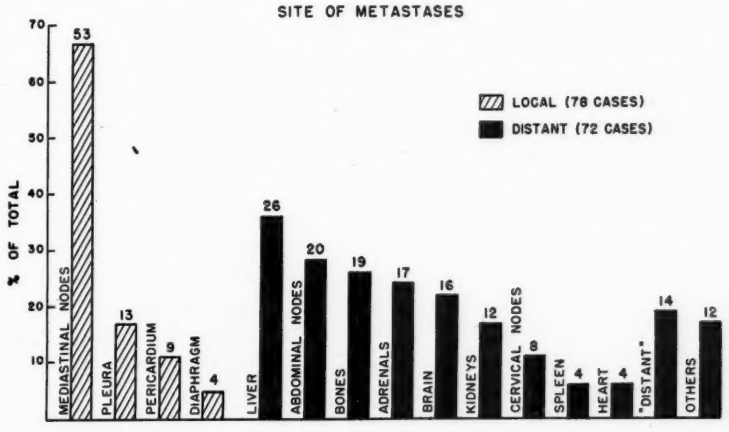


Fig. 28.

Four routes of spread are recognized: (1) local invasion by contiguity, (2) lymphatic, (3) blood stream, and (4) bronchiogenic dissemination. Local extension is universally recognized and it is not unusual for this tumor, which

frequently attains a massive size, to extend locally until an entire lung is involved. In these cases the pulmonary architecture is well preserved despite the total involvement with tumor. This finding is in distinct contrast to the growth characteristics of carcinoma of bronchial origin, a neoplasm which is typically destructive in nature. It has been predicated that in bronchiolar carcinoma the tumor spreads from alveolus to alveolus by way of the pores of Cohn.[19, 20, 73] Lymph-borne spread is undisputed, having been established in 38 per cent of 205 patients. We have repeatedly observed tumor emboli in the pulmonary lymphatics, as have Fried,[35] Silverman and Angrist,[20] Laippley and Fisher,[32] and many others. The perivascular and peribronchial lymphatics are found to be dilated and often filled with tumor cells. The evidence to support the occurrence of metastases by the blood stream is unequivocal. We have been able to demonstrate malignant cells in the pulmonary vascular channels and similar findings have been recorded by Fried,[35] Laippley and Fisher,[32] Tillett and Hirsch,[74] and Gepts.[75] Thirty-five per cent of 205 patients showed distant metastases. The liver, abdominal nodes, bones, adrenals, brain, and kidneys were the most frequent sites of distant spread, in that order. It is clear that these distant metastases were most often blood borne. There remains for consideration the question of bronchiogenic dissemination or so-called aerial metastases.[19, 59, 73, 76] This matter is of critical importance in a consideration of these tumors. If this thesis is accepted, it will readily explain the frequency of bilateral lesions, with spread from a primary focus in one lung to the opposite lung, often without involvement of the mediastinal lymph nodes.

The theory of multicentric origin of these new-growths, which has never been adequately substantiated despite intensive study by many pathologists over a long period of years,[10-12, 35, 42] might be abandoned if the concept of spread via the air passages can be proved. Conviction that these tumors arise unicentrically would make it logical to offer patients with this disease a far more hopeful outlook than that which they are now accorded. Furthermore, acceptance of aerial metastasis as a frequent means of spread would probably influence the type of surgery performed in patients with this tumor. It has been shown that 46 per cent of patients with bronchiolar carcinoma have no metastases, even at the time of death. An additional 15.6 per cent show *distant metastases only,* and 19.5 per cent demonstrate both local and distant spread. Eighty-one per cent of all patients therefore would receive no real lasting benefit from radical surgery of the type customarily employed in treating carcinoma of bronchial origin. Bronchiogenic cancer of course behaves in quite a different manner. In that neoplasm, spread to the mediastinal nodes is commonly an early finding and almost invariably occurs sooner or later. Metastases to the opposite lung, on the other hand, is rather infrequently seen. Schuster[76] has observed that it is only to be expected that malignant cells should be inspired into the air spaces and there set up multiple deposits on the alveolar walls. Silverman and Angrist[20] studied two cases of bronchiolar carcinoma and concluded that the tumor nodules dispersed throughout the parenchyma were obviously metastatic. Watson and

Smith[58] stated that metastases were most frequent to the same lung, the opposite lung or hilar nodes. Others[77, 78] have expressed the same opinion. Frissell and Knox[73] have mentioned the possibility of spread by bronchiogenic dissemination as have many others. Papillary projections which break off easily are characteristic of this disease and the loose attachment of the tumor cells lining the alveoli has been repeatedly demonstrated. The fact that they desquamate and are coughed up has been proved numerous times by studies of the sputum by the Papanicolaou method.[10, 52, 58, 72] Herbut[18] has been one of the strongest proponents of the unifocal origin of bronchiolar carcinoma and has offered evidence to support his position that is difficult to refute.

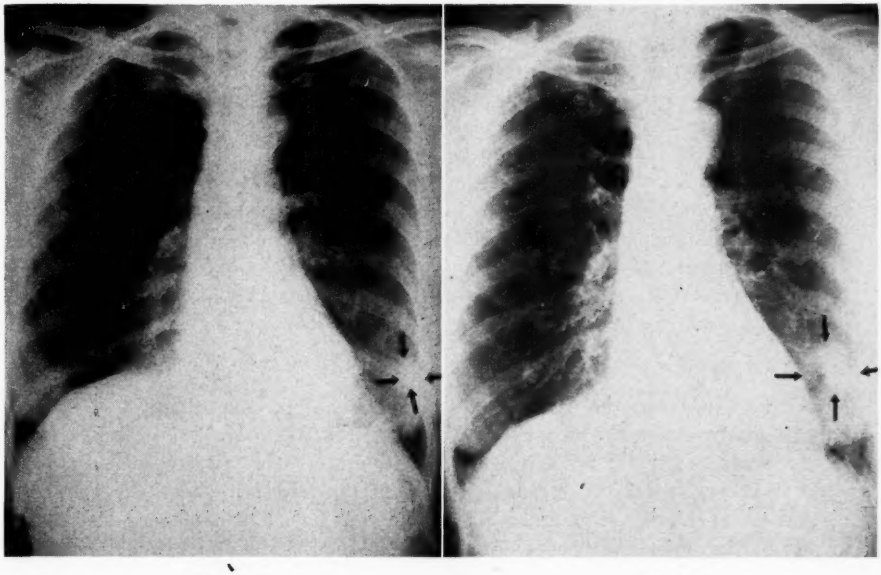


Fig. 29. Fig. 30.

Fig. 29.—Chest x-ray film of a 72-year-old white woman made in 1946 showing a small but definite infiltrate in the left lower lung field.

Fig. 30.—Chest roentgenograms of the same patient made in 1950. The lesion seen in Fig. 30 has definitely increased in size but remains well localized. Resection of the left lower lobe showed bronchiolar carcinoma. The patient is alive and apparently well three years later.

Stewart[34] questions the apparent multiple origin of bronchiolar carcinoma and believes that multiple foci are due rather to lymphatic spread from a single focus with subsequent lining of lung acini. Weller[21] is of the same opinion. Tillett and Hirsch[74] have been able to demonstrate the source of malignant tumor emboli which spread to both lungs by way of the pulmonary artery. They concluded that the concept of a multicentric origin of these tumors of the lung should be discarded. There are gross and microscopic features in this disease, however, that make it difficult if not impossible to explain all metastases on the basis of either blood-borne or lymphatic dissemination. In a painstaking study recently reported, Hutchinson[19] offers

convincing evidence that the distribution of the tumor within the lung is determined by the air passages. He feels that the case which he studied in minute detail "not only establishes the extra-alveolar origin of some, at least, of the group of so-called alveolar-cell tumors but prove also that these growths may metastasize via the air passages." Aerial metastases, in addition to spread by the blood and lymph channels, appears to be a much more logical explanation of the behavior of this neoplasm than the unproved theory of multicentric origin. The late appearance of new lesions in the same or opposite lung following unilateral subtotal pulmonary resection or in the contralateral lung after total pneumonectomy can by no means be accepted as proof of a new primary lesion. One patient reported in this series presented conclusive x-ray evidence of a lesion four years before it was resected (Figs. 29 and 30) and proved to be a bronchiolar carcinoma. Even at the time of resection it was small and localized. How long it was present before its demonstration by chest roentgenograms is of course indeterminate.

Another patient's lesion, a small, circumscribed, peripheral nodule, remained stable at least twenty months and quite possibly considerably longer (Fig. 1). The known duration of the disease has been at least seven or eight years[63] and probably longer (eleven to fifteen years) in a number of cases.[62, 79] In view of the frequent indolent behavior of these lesions, it would not seem illogical to assume that tumors which make their appearance months or years following resection usually represent metastatic lesions which were present but undetected at the time of operation rather than having arisen *de novo*.

TREATMENT

Until very recently, the diagnosis of bronchiolar carcinoma was made only at autopsy. In the rare case in which it was established during life, the disease was usually far advanced and only symptomatic and supportive treatment were employed. Numerous patients in the past have been erroneously diagnosed as having tuberculous and treated for that disorder; the true nature of the illness was revealed only at post-mortem examination. Irradiation and cytotoxic agents, such as nitrogen mustard, have been used in a few cases without proved beneficial results. Most authors who have reported upon the use of x-ray therapy have stated that it is completely useless in this malignancy.[15, 50, 51] Within the past few years, resection has been employed with increasing frequency. This can be attributed to more accurate diagnostic methods, particularly cytologic studies of the sputum in patients with this disease, and to an increasing tendency on the part of the profession to advise prompt thoracotomy in space-occupying pulmonary lesions of uncertain etiology. There is a mounting awareness that "unresolved pneumonia" often means cancer and a laudable decrease in the tendency of physicians to "watch" undiagnosed pulmonary infiltrates that could reasonably represent carcinoma.

As a result of this aggressive policy, 49 patients with this rather uncommon pulmonary carcinoma have been treated by resection within the past seven years. Hope for patients with this lethal disease lies exclusively in *early* excisional surgery. In order that resection may offer reasonable pros-

pects of a cure, operation must be undertaken while the tumor is still localized and before the correct diagnosis may be made or strongly suspected on clinical grounds. If one waits until the clinical picture which some have considered as classic or typical is presented, the patient's fate is sealed. The mode of metastases of this tumor might well influence one to perform limited resection when surgery is undertaken. Whether it is of multicentric origin or arises in a single focus from which it may spread, it does not seem logical to advocate total pneumonectomy for bronchiolar carcinoma except in those patients where the unilateral distribution of the lesions makes that operation mandatory. If this malignancy does take origin from multiple primary foci, the advisability of employing surgery at all in its management might well be questioned.[14, 19]

That very question has been, in fact, raised before the American Association for Thoracic Surgery in the recent past.[80] If, on the other hand, it is of unicentric origin and spreads by bronchiogenic dissemination as well as by more conventional routes, it would be difficult to defend a policy of routine radical surgery in its management. If an undetected metastasis has occurred prior to operation, the surgeon cannot divine the site to which the tumor has spread. It has been shown that but 19 per cent of patients with this disease will show metastases confined to the mediastinal nodes, while almost as many (15.6 per cent) will show distant spread only and 19.5 per cent will have both local and distant metastases. It is of course not possible to determine the percentage of spreads to the opposite lung, not yet visible by x-ray examination, which will have occurred at the time of excisional surgery. In view of the high percentage of patients who ultimately show bilateral pulmonary involvement, there seems to be little doubt that this circumstance will occur rather frequently.

Although we have treated one patient by segmental resection who shows no evidence of recurrence one and one-half years later and Watson and Smith[58] report a patient who is alive and well more than five years after "V" excision of a bronchiolar carcinoma, the frequency with which we and others[13, 17, 56, 67] have found tumor involvement of the pulmonary lymphatics have led us to conclude that lobectomy is the treatment of choice in these patients when the distribution of the disease makes that operation feasible. There appears to be ample reason, in view of the nature of this tumor and the manner by which it appears to spread, to restrict resection of localized bronchiolar carcinoma to a reasonable minimum. The presence of mediastinal nodes showing histologic evidence of malignancy on examination of frozen sections in a patient without clinical or radiographic evidence of spread elsewhere would obviously call for a total pneumonectomy and radical mediastinal node dissection. Fig. 31 shows the treatment employed in 155 patients. Of the 49 patients who have undergone resection, 24 have been treated by lobectomy; pneumonectomy has been performed in 18; segmental resection in 4 and local enucleation in 3. Right lower lobectomy was performed at the original operation in one case but the tumor recurred three years later and the remainder of the right lung was removed. One of the lobectomy patients

underwent bilateral operations, a left upper lobectomy being followed after a short interval by right upper lobectomy and local resection of a segment of the right lower lobe. One of the patients treated by segmental resection of an upper lobe segment also had local enucleation of a rounded lesion from the lower lobe on the same side. That patient had a recurrence in the lower lobe four months later and lower lobectomy was performed for the recurrent lesion.

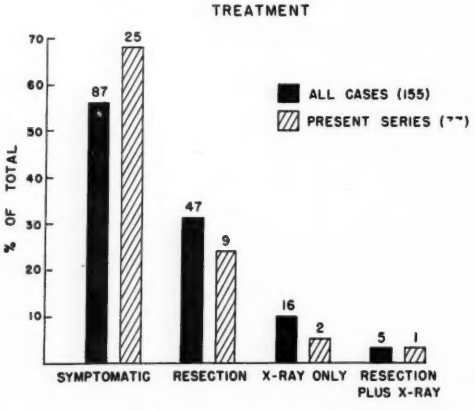


Fig. 31.

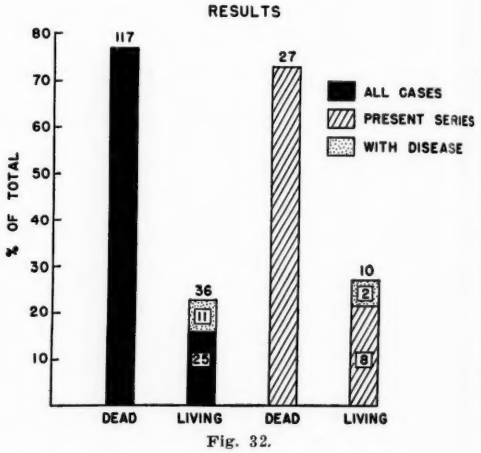


Fig. 32.

Investigation of the fate of the 49 patients who had resections reveals that those who have been treated by lobectomy or lesser operation have fared somewhat better than those who underwent pneumonectomy. The patients who had conservative surgery no doubt constituted a more favorable group with generally smaller more localized lesions. We are certain of 5 patients who are alive and well more than five years after resection; 2 of these have been reported by Watson and Smith,[58] and one case each by Skorpil,[60] Osserman and Neuhof[81] and Delarue and Graham.[40] Four of these patients were managed by lobectomy and the other had a wedge resection. Graham's patient later had the remaining lobes of the right lung removed. Two patients in our series who were treated by lobectomy are alive and well over three years postoperatively, and one man who had a segmental resection is clinically and radiographically free of disease one and one-half years after surgical treatment.

RESULTS

Information as to the results of treatment was available in 153 of the 155 patients who were analyzed from the standpoint of therapy. The results are listed in Fig. 32.

In this graph, patients have been listed as living and well or living with disease on the basis of the last follow-up information. The fatal course of bronchiolar carcinoma is clearly shown by the fact that 77 per cent of the

patients have already died and death from the disease is anticipated in at least an additional 7 per cent. It is important to remember, however, that potentially effective therapy has been employed in patients with this neoplasm only in very recent years.

FOLLOW-UP

An attempt has been made to obtain follow-up information on the 36 surviving patients. The available data are tabulated in Fig. 33.

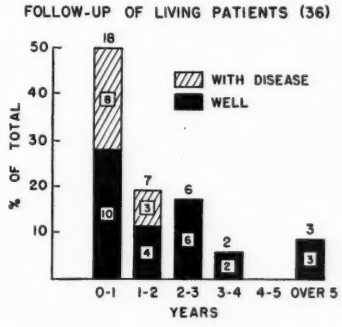


Fig. 33.

Recent follow-up information has not been available on many patients. The survival time listed in this graph is dated from the time of operation or other treatment to the date of the last follow-up. The most interesting finding in the follow-up study was the fact that all of the patients living with disease fell into the group who had been followed two years or less after surgical treatment. None of the patients followed longer than two years showed recurrent or persistent disease. This would suggest that recurrent tumors lead to a fatal termination within less than two years and, conversely, that patients who survive without evidence of disease for more than two years are likely to remain well. The number of patients followed is too small, of course, for definite conclusions to be drawn.

SUMMARY

The literature pertaining to an unusual pulmonary neoplasm, known variously as bronchiolar carcinoma, pulmonary adenomatosis, alveolar-cell tumor, alveolar-cell carcinoma, and by numerous other similar terms, has been reviewed. The histogenesis, pathology, clinical features, diagnosis, and treatment have been discussed. Thirty-seven hitherto unrecorded cases of this entity are reported. The reports of 120 patients with bronchiolar carcinoma which have appeared in the literature since the article by Swan[13] have been abstracted. One hundred eight of the collected cases and the 37 cases reported have been statistically analyzed. The essential data on the 37 patients reported herein are included in Table I. Similar data on the 120 patients collected from the literature are to be found in Table II.

TABLE I. STOREY,

PATIENT AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
1. B. J. R. A.F.I.P. Acc. No. 143162 1945	53	W	M	6	Anorexia, vomiting. Pain in head, neck, shoulders	Cherry-sized lesion in right upper lobe and right lower lobe	Amount not noted. Not examined
2. C. B. H. A.F.I.P. Acc. No. 167099 1945	77	W	F	12	Intermittent dyspnea and fatigue for 12 mo. Nonproductive cough. Pain in right shoulder	Complete clouding of right lung	Not examined
3. E. A.* V. A. Hospital, Louisville, Ky. 5165 1946	53	W	M	5	Dyspnea. Lower chest pain, bilateral	Miliary soft infiltrations in both lung fields	Fungus isolated 1 wk. prior to death. Negative for AFB
4. F. S. A.F.I.P. Acc. No. 189063 1947	53	W	F	3	Onset Jan. 1947 with pain in chest and dyspnea; cough with copious frothy sputum. Dec. 1946 nausea and vomiting, anorexia and weight loss	Disseminated miliary-like patches throughout all lung fields	Negative for TBC. Cryptococcus found
5. J. H. W. A.F.I.P. Acc. No. 206491 1947	60	W	M	60	Onset 1942 with cough, occasional hemoptysis dyspnea on exertion; intermittent dull, left-sided chest pain	Opacity in lingula of left upper lobe	Negative for TBC
6. S. L. A. A.F.I.P. Acc. No. 215026 1947	40	W	M	1	Hemoptysis, dyspnea, pain in right chest. Cough, severe, became paroxysmal, more blood, then better. One month later symptoms returned and patient went downhill	Right hydropneumothorax. Only air-bearing tissue in right apex	Negative for AFB, fungus and Papanicolaou negative
7. V. D. L. A.F.I.P. Acc. No. 186230 1947	35	W	M	4	Gradual onset of right chest pain posteriorly, cough, dyspnea, excessive fatigue, weight loss. Tentative diagnosis: tuberculosis, then changed to malignancy when wine colored fluid obtained from chest	Pleural effusion right hemithorax obscuring lung markings	Negative for AFB
8. E. F. McC. A.F.I.P. Acc. No. 204693 1947	65	W	M	7	Cough, dyspnea, sputum streaked with blood (copious amount of sputum, yellowish-white). Anorexia and history of hemoptysis and ASCVD with myocardial infarction	7 cm. mass in left lower lobe with atelectasis. Emphysema, left upper lobe	Smear and culture neg. repeatedly for AFB and fungi

KNUDTSON, AND LAWRENCE

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Autopsy	Bronchiolar carcinoma	Right lower lobe	Right hilar nodes, pia-arachnoid, medulla and cord	Insulin and diet (for diabetes). Supportive. Irradiation (head)	Adm. 4/26/45 Died 5/23/45
Autopsy	Bronchiolar carcinoma	Entire right lung. Primary was in right apex	Chest wall, hilar nodes, heart	Supportive only	Adm. 11/1/45 Died 12/15/45 (Prev. Hosp. in Aug. '45. Diag.: Neurofibroma)
Autopsy	Bronchiolar carcinoma	All lobes, both lungs	Hilar lymph nodes	Supportive	Adm. May, 1946 Died 6/17/46
Autopsy	Bronchiolar carcinoma	All lobes, both lungs	None	General therapy. Two 125 r x-ray irradiations	Adm. 2/26/47 Treatment: 250 roentgen u. Died 3/3/47
Surgical specimen	Bronchiolar carcinoma	Lingula, left upper lobe	None	Left thoracotomy and amputation of lingula	Alive with no evidence metastasis Jan. '50
Thoracotomy and autopsy	Bronchiolar carcinoma	Right middle lobe almost solid. Nodule in upper and lower lobes, rt.	Pleura bilaterally. Tracheobronchial lymph nodes	Rt. thoracotomy, inoperable, closed. Supportive therapy	Adm. 8/1/47 Home with inoperable Ca 3 mo. Re-adm. 1/12/48. Died 1/15/48
Autopsy	Bronchiolar carcinoma	Right lung, all lobes	Supraclavicular, paratracheal and hilar lymph nodes; liver, both adrenals, kidneys, cerebrum, skin (abdominal wall), retroperitoneal and mesenteric lymph nodes	Investigative studies incl. biopsy of cervical node and skin nodule on ant. abdominal wall. Supportive therapy	Adm. 12/28/46 Died 3/12/47
Autopsy	Bronchiolar carcinoma	Upper and lower lobes. Predominately in left lower lobe	Pleura, supraclavicular, mediastinal, and hilar lymph nodes	Supportive therapy. Treated for CVD and infarction	Died three mo. after admission

TABLE I.

PATIENT AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
9. G. B. A.F.I.P. Acc. No. 211674 1947	52	W	M	4	Increasing cough, weight loss, shortness of breath, and recent onset of weakness and fever. Pneumonia and tuberculosis diagnosed first, then changed to malignancy	"Consolidation right base and innumerable nodular densities throughout both lung fields"	Negative for AFB
10. R. J. M. A.F.I.P. Acc. No. 289061 1948	39	W	M	11	Sudden onset of left pleuritic pain, chills, fever and cough (rusty sputum). Improved on bed rest and penicillin but 11 mo. later noted cough, weakness, large amounts sputum, dyspnea	Large amount fluid on left. Extensive mottling on right at level of second, third, and fourth interspaces. Aeration in apex right upper lobe, and middle lobe	Repeatedly negative for AFB. Up to 7 pints per day. Hemolytic strep. culture
11. C. J. S. A.F.I.P. Acc. No. 217750 1948	42	W	M	2	Progressive shortness of breath and dull aching in rt. lower chest. Pt. visited T.B. center. X-ray showed pulmonary path., then admitted to hosp.	On Adm.: Heavy nodular infiltration widely scattered throughout both lung fields. Subsequent: Incr. in nodular infiltration	Negative for AFB, fungus. Papanicolaou negative
12. H. P. B. A.F.I.P. Acc. No. 260163	61	W	M	12	Coughing up blood. Cough for one yr., nonproductive at first but later increasing cough productive of reddish sputum. Weight loss, weakness, anorexia	Density in left upper chest suggestive of malignancy. Suspicious lesion in right upper lobe also	Repeatedly negative smear and culture for AFB
13. J. E. P. A.F.I.P. Acc. No. 317202 1948	57	W	M	30	Progressive orthopnea and weight loss. Dyspnea, productive cough. Pain right scapula, right lower chest and right upper quadrant	Extensive infiltration through entire left lung and almost complete collapse of right lung. Pneumothorax, rt. Fractured tenth rib, right midaxillary line	Papanicolaou negative on several occasions. Sputum negative for AFB
14. J. T. T. A.F.I.P. Acc. No. 285263 1949	61	W	M	24 to 36	Increasing shortness of breath, weakness, morning cough productive of 1-2 tablespoons yellowish sputum. In 6 mo., increasing weakness, 35 lb. weight loss, more productive cough, anorexia	Mild bilateral emphysema. Extensive reticulated and cavitary infiltrations in left upper lobe and right lower lobe	15 cultures negative for AFB

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Autopsy	Bronchiolar carcinoma	Right lower lobe	Hilar and mediastinal lymph nodes, scalp, liver, skeletal of skull T_{10}	Pneumonia treated with penicillin; fever disappeared with incr. dyspnea and downhill course: Supportive therapy	Died two mo. after admission
Autopsy	Bronchiolar carcinoma	All lobes; LLL solid, others—nodules ½ cm. to 3 cm.	None	"5 deep x-ray treatments to ant. chest." Iodides, acriflavin, penicillin for fungus	Respiratory death 17 days after admission
Autopsy	Bronchiolar carcinoma	All lobes	Peribronchial and periaortic nodes. Both kidneys	Supportive	Died two mo. after admission
Autopsy	Bronchiolar carcinoma	Left upper lobe	Left anterior chest wall and second left rib anteriorly. Heart, liver, spleen, intestines, adrenals, kidney, and mesentery	Supportive	Died 6 days after admission
Autopsy	Bronchiolar carcinoma	All lobes, bilateral	None	Palliative	Died 20 days after admission
Autopsy	Bronchiolar carcinoma	Left upper and lower lobes, lower predominantly (none in right lung)	Hilar lymph nodes, left	Streptomycin, 1 Gm. q6h for 15 days. Aureomycin, penicillin, streptomycin for peritonitis	Died 2½ mo. after adm. of intestinal obstruction

TABLE I.

PATIENT AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
15. O. C. B. A.F.I.P. Acc. No. 203244 1949	73	W	M	8	Hacking cough (paroxysmal 5-10 days apart), productive of slight mucoid, blood-streaked sputum. Severity and frequency of cough increased, dyspnea, low-grade fever, left pleuritic pain, and weight loss one mo. prior to admission	Infiltration of left lower lobe. Probable 2.5 cm. mass below left bronchus	Negative for AFB. No other organisms cultured
16. F. A. T. A.F.I.P. Acc. No. 276201 1949	23	W	M	8	Increasing shortness of breath; 4 mo. later noted weakness and dyspnea and dull pain in right lower chest anteriorly (later on left also). Weight loss and cough with moderate whitish sputum, occasionally blood streaked	On admission: Fluid, right; nodules, left. Later: Density, right middle lobe, nodules all other lobes. Moderate-sized cavity, left upper lobe	Negative for AFB and fungi. No Papanicolaou recorded
17. E. L. P. A.F.I.P. Acc. No. 269237 1949	59	W	M	4	Sharp low back pain, weakness, 40 lb. weight loss, nocturia, nausea and vomiting; chronic cough with very little sputum	Chest x-ray showed circumscribed density in left lower lobe. Spine films showed destruction of L-2	Negative for acid-fast bacilli. Positive Papanicolaou for malignancy
18. J. J. M. Naval Hospital, St. Albans, N. Y. No. 109054 1949	37	W	M	10 days	Cough (dry) for 6-7 months. Slight ache in chest (anterior) of indefinite duration	2 cm. density of left upper lobe in third interspace	Negative for acid-fast bacilli
19. P. O. K. A.F.I.P. Acc. No. 296049 1949	54	W	M	2	Abdominal pain; ulceration of left foot	Homogeneous density in region of left lower lobe. Mass in apex of left lung	Negative for acid-fast bacilli
20. J. C. A.F.I.P. Acc. No. 264139 1949	75	W	F	31	Cough, dyspnea, expectoration, loss of weight, anorexia	Triangular area of infiltration opposite right hilum; smoky infiltration, lower three-fourths, left chest	Clear, watery. Negative for AFB and fungi
21. L. M. A. A.F.I.P. Acc. No. 276486 1949	40	W	M	4	Shortness of breath, weakness, weight loss	Entire left chest obscured by homogeneous density; scattered rounded shadows throughout right lung	Meager amount. Positive Papanicolaou
22. K. B. A.F.I.P. Acc. No. 337939 1950	72	?	F	—	No symptoms. Accidental discovery on routine x-ray	Round nodule 4-5 cm. in diameter, posterolateral aspect, right lower lobe	None

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Autopsy	Bronchiolar carcinoma	LLL. Large nodule compressing bronchus. Diffuse nodular involvement of rest of lobe (lt. lower with areas of necrosis)	Liver and vertebrae (L-1 and L-2)	Considered for x-ray irradiation but none given	Died 3 wk. after admission of respiratory death
Autopsy	Bronchiolar carcinoma	All lobes, both lungs	Pleura, pericardium, diaphragm, liver, both kidneys, lt. adrenal, cerebral and cerebellum meninges, third lumbar vertebra; peribronchial, peritracheal, periaortic and perigastric lymph nodes	Supportive	Died one mo. after admission
Autopsy	Bronchiolar carcinoma	Left lower lobe	Hilar and mediastinal nodes, all lumbar vert., both adrenals, liver, kidneys, gut, esophagus, spinal cord, brain and meninges	Supportive	Died 9 mo. after admission
Surgical excision frozen section (thoracotomy)	Bronchiolar carcinoma	Left upper lobe	None	Thoracotomy, lt., with lt. upper lobectomy (curative)	In good condition 6 mo. later
Biopsy (bronchial)	Bronchiolar carcinoma	Left lower lobe	Regional tracheobronchial and bronchial nodes, bilateral adrenals, cerebral and cerebellar regions	Palliative	Died 5½ mo. after admission
Uncertain. Apparently at autopsy	Bronchiolar carcinoma	Indefinite (see x-ray report). Apparently both lungs	Data not available	Supportive only	Died
Positive Papanicolaou. Positive bronchial. Needle biopsy. Autopsy	Bronchiolar carcinoma	Both lobes, lt. lung solid tumor, wt. 1,100 Gm. All lobes rt. lung contain innumerable round, discrete nodules, wt. 1,275 Gm.	None	Palliative	Died 1¾ mo. after admission
Resection	Bronchiolar carcinoma	Lateral segment, left lower lobe	None	Left lower lobectomy	Well with neg. chest x-ray 3 yr. P.O.

TABLE I.

PATIENT AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
23. S. H. A.F.I.P. Acc. No. 303099 1950	57	N	M	?	Mild dyspnea, right-sided chest pain, productive cough, mild anorexia, generalized weakness	Infiltrating lesion of right upper lobe	Negative for AFB, fungus and malignant cells
24. J. B. A.F.I.P. Acc. No. 307704 1950	67	W	M	?	Persistent cough	"Indefinite" infiltration of right upper lobe	Negative for malignant cells
25. J. J. A.F.I.P. Acc. No. 308751 1950	60	W	M	1	Head cold followed by severe cough and dyspnea, productive of ½ cup yellowish-gray sputum; no hemoptysis. Had to sleep in sitting position. 15 lb. weight loss. Local doctor bronchoscoped and found malignant cells	Small area of clouding just above and lateral to superior portion of right hilum. Lateral view shows consolidation in basal portion of right upper lobe	Negative for AFB. Positive for malignant cells
26. U. S. E. A.F.I.P. Acc. No. 297974 1950	58	W	M	1	Mental confusion, speech difficulty, and irritability for one mo.	None taken	Negative for malignant cells
27. L. S. A.F.I.P. Acc. No. 319700 1950	71	W	M	7	Pain in flank, chest, and shoulder on right. Paroxysmal cough productive of thick, copious sputum, occasionally blood streaked; weight loss, febrile episodes, weakness, and incr. dyspnea	Homogeneous density in lower half of right lung field	Negative for AFB and malignant cells
28. W. J. T. A.F.I.P. Acc. No. 311563 1950	52	W	M	2-3 wk.	Hemoptysis (8 days prior to admission). Slight dyspnea on exertion. 10-12 lb. weight loss	Area relative uniform density, lower ⅓ left lung field; bronchial margins partially visualized	Neg. for AFB. (2 exam. of bronchial secretion neg. for cancer cells)
29. J. N. H. Naval Hospital, St. Albans, N. Y. No. 116208 1950	24	W	M	4	Burning sensation under right scapula, 4 mo. Dry cough for 2-3 mo. Low back pain with radiation to right leg, 4 mo.	Nodular density in third right interspace 10/21/50. Similar findings on film of 6/21/49. Read as negative	Neg. for AFB. Several suspicious Paps. (Class III)
30. F. E. A.F.I.P. Acc. No. 307136 1950	27	W	M	24	Dry cough for 2 yr.; dyspnea with generalized pains over entire body	Rounded density in right mid-lung field short distance from hilum	Three 24-hour sputum specimens negative for neoplastic cells
31. G. Y. A.F.I.P. Acc. No. 507262 1951	54	N	M	16	Cough productive of blood-streaked sputum. Weakness, dyspnea, left chest pain, weight loss	Diffuse and extensive nodular infiltration both lungs, more marked on right	Amount not stated. Not examined for AFB or malignant cells
32. W. C. C. A.F.I.P. Acc. No. 508899 1951	45	W	M	4½	Productive cough, loss of weight, easy fatigue	Complete opacity of entire left lung field	"Much." Negative for AFB

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Surgical specimen	Bronchiolar carcinoma	Right upper lobe	Hilar lymph nodes extensively involved	Thoracotomy, right with right pneumonectomy	No cough, sputum, dyspnea, 2 mo. P.O.
Surgical specimen	Bronchiolar carcinoma	Right upper lobe	None	Thoracotomy with right upper lobe lobectomy	
Surgical specimen	Bronchiolar carcinoma	Right upper lobe	None	Thoracotomy, right with pneumonectomy	Alive 1½ yr. P.O.
Autopsy	Bronchiolar carcinoma	Right lower lobe (periphery)	Brain, hilar lymph nodes	Craniotomy but no tumor found	Died one day P.O.
Autopsy	Bronchiolar carcinoma	Right middle lobe, right lower lobe, right upper lobe	Parietal pleura, mediastinum, epicardium, both adrenals	Palliative and symptomatic therapy	Died 14 days after admission
Surgical specimen	Bronchiolar carcinoma	Left lower lobe	None	Left lower lobe lobectomy	Symptom free last follow-up
Lung biopsy via thoracotomy	Bronchiolar carcinoma	Right upper lobe	Heart, liver, kidneys and spine	Thoracotomy, right, with biopsy. Supportive, with x-ray to spine	Died 4½ mo. after admission
Rt. pneumonectomy	Bronchiolar carcinoma	Right hilar region of right lung	Osteolytic lesion, left ilium	Rt. pneumonectomy. X-ray treatment to left ilium	Alive with metastatic disease
Autopsy	Bronchiolar carcinoma	All lobes, both lungs, worse on right	Tumor was seen in lymphatics and blood vessels of lung	Digitalis. Penicillin	Died 12 hr. after admission
Autopsy	Bronchiolar carcinoma	Both lungs: lt. solid. Wt. lt.—1,300 Gm. Wt. rt.—850 Gm.	Ribs, dorsal spine, pericardium, diaphragm, liver. No positive nodes	O_2, antibiotics, streptomycin, blood transfusions	Died 41 days after admission

TABLE I.

PATIENT AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
33. L. S.† Mound Park Hospital, St. Petersburg, Fla. No. T-7504 1951	63	W	F	24	Chest pain, 2 yr. debility, weakness, emaciation, nonproductive cough	Dense opacification, left lung. Bilateral pleural effusions (bloody)	Sputum and pleural fluid repeatedly neg. for AFB. Sputum pos. for atypical cells. Pap. Class III
34. B. S. H. Naval Hospital, St. Albans, N. Y. No. 120251 1951	44	W	M	10	No symptoms. Discovered on routine chest-x-ray, Dec., 1950. In April, 1951 developed productive cough and pain, right upper chest, anteriorly	Small, smooth, round, circumscribed lesion, 2.5 cm. in diameter, anterior segment, right upper lobe	8 sputum cultures neg. for AFB. Papanicolaou not done
35. C. H. B.‡ V. A. Hospital, Seattle, Wash. No. 67-715 1951	74	W	M	?	Dyspnea, motor aphasia. Right hemiplegia	Small irregular infiltrations scattered throughout lower one-half of left lung	Gastrics negative for AFB. (Patient was not rational and sputum could not be collected.)
36. N. L. F.§ Naval Hospital, Portsmouth, Va. No. 127237 1952	42	W	F	9	No symptoms. Discovered on routine chest x-rays. Later developed slight dyspnea on exertion	Diffuse bilateral millinodules, all lobes, both lungs	Negative for AFB. Papanicolaou negative. Negative for fungi
37. J. H. Naval Hospital, St. Albans, N. Y. No. 130549 1952	23	W	M	31	Productive cough, repeated small hemoptyses, right chest pain, 9 pound weight loss	Large rounded homogeneous density in right lower lobe; irregular small homogeneous density in anterior segment, right upper lobe	Small amount of mucoid sputum with several small hemoptyses; later: 60 c.c. mucoid sputum daily with occ. blood

*Case included through the courtesy of Drs. Harold Gordon, J. R. Gott, Jr., and R. A. Switzer.

†Case included through the courtesy of Drs. E. B. Campbell, Sr., and E. B. Campbell, Jr.

‡Case included through the courtesy of the Medical Director, United States Public Health Service Hospital, Seattle, Wash.

§Case included through the courtesy of Drs. Charles Ferguson and Paul Spangler, U. S. Naval Hospital, Portsmouth, Va.

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
1. Suspicious Pap. 2. Definitive: Autopsy	Bronchiolar carcinoma	Both lungs. Pleura diaphragm, peritoneum	Pleura, diaphragm, peritoneum, mesentery	Supportive and symptomatic only	Died 4 mo. after admission
Segmental resection	Bronchiolar carcinoma	Anterior segment, right upper lobe. Hilar nodes neg.	None	Segmental resection anterior segment, right upper lobe	Well 18 mo. after resection
Autopsy	Bronchiolar carcinoma	Left upper lobe, small foci, left lower lobe	1. Brain—2 foci, left cerebral hemisphere. 2. Posterior pituitary (?).	Symptomatic. Penicillin, oxygen, etc.	Died approximately two mo. after admission
Lung biopsy, left lower lobe	Bronchiolar carcinoma	All areas, all lobes, both lungs. (Extensive pleural invol. many nodules)	None	Symptomatic	Adm. 3/24/52. Still in hospital. Disease rap. progress
Resection	Bronchiolar carcinoma	Medial basal segment, right lower lobe and anterior segment, right upper lobe METASTASES	None evident at operation. Nodes negative. Recurrence in right lower lobe 4 mo. later	Segmental resection anterior seg., RUL and local enucleation of lesion, RLL. Right lower lobectomy for recurrent lesion four months after original operation	No evidence of disease at present (9 mo. after second operation)

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
1. Skorpil[60] 1941	34	W	M	About 30 mo.	Sensation of pressure in left chest	A spherical, homogeneous shadow, size of a mandarin, seen in the middle of left lung field next to upper portion of hilum. Thought to represent metastatic spread to hilar nodes from a small primary lesion barely visible in upper lobe	1 episode of hemoptysis
2. Acevedo, Giuntini, and Croxatto[65] 1942	50	W	F	14 mo.	Weakness, anorexia, dyspnea on exertion, slight cough productive of yellow sputum, orthopnea	Multiple nodular soft confluent densities in right lung. 6 mo. later: Lt. hydropneumothorax with no change on right side. Also had homogeneous opacity, lower and middle portions, left lung field	Mucopurulent, viscous and transparent sputum up to 1,500 c.c. daily
3. Fernandez Luna and Bracco[61] 1943	62	W (Argentinian)	M	8-9 mo.	Febrile episode (grippe) with much sputum. Pain in right upper chest, cough, sputum, weight loss	Opacity, right upper hemithorax with cavitation in mid-lung field	Purulent, copious, bloody. Free AFB by smear and G.P. inoculation
4. Wenger[7] 1945	60	W (Bolivian)	F	Several mo.	Cough of several mo.; 1 mo. prior to death, cough increased, febrile. 15 days before death, intense cough and high fever	Not done	Not mentioned
5. Couch, Fleming, and Harrison[82] 1945-47	48	W	F	Unknown	Pain in shoulder and lumbosacral region	Not done	Not recorded
6. Rey and Rubinstein[56] 1947	62	W	M	8½ mo.	Cough, mucopurulent, viscous, and transparent sputum up to 1,500 c.c. daily. No fever and general health unchanged. No weight loss	Localized lesion in right base, and incr. lt. hilar shadow. Last x-ray 1 mo. prior to death showed increase of right basal and left hilar process	Small quantity of yellow-green sputum
7. Silverman and Angrist[20] 1948	31	W	F	6 mo.	Pleuritic pains, right chest. Shortness of breath and cough	Initially, evidence of consolidation of the right lower lobe, later involvement on the left side also	Character not stated. "Scanty"

COLLECTED CASES

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Resection	Alveolar epithelial carcinoma	Peripherally in left upper lobe	None	Left upper lobe lobectomy	Alive and well 5 yr. later
Needle biopsy	Bronchorrheal form of gelatinous cancer of the lung	Right lower lung field and left hilar region	None noted (no autopsy)	Symptomatic	Dead
Post-mortem	Pseudopneumonic pulmonary cancer (Ewing's diffuse alveolar cancer)	Right lung	None	None	Dead
Post-mortem	Alveolar-cell tumor	All lobes, both lungs	Liver	None	Dead
Post-mortem	Alveolar-cell tumor	2 by 2 cm. nodule in LUL	Liver, both adrenals, brain and vertebrae	Symptomatic	Dead 3 mo. after adm.
Papanicolaou	Pulmonary adenomatosis	Entire right lung and lower half, left lung	None	Symptomatic	Dead
Post-mortem	Lobar adenocarcinoma	Bilateral	Hilar nodes, adrenal glands, kidney	None	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
8. Silverman and Angrist[20] 1948	73	W	F	2 mo.	Cough and bloody sputum	Increased density lower half rt. lung, incr. density and prominent radiating shadows upper lobe rt. lung, prominent bilateral hilar shadows. 2 wk. later: Radiating shadows entire rt. lung, prominent bilat. hilar shadows, nodular infiltrations throughout rt. lung. Pleural eff., rt.	Bloody
9. Hildebrand[83] 1948	66	W	F	9 mo.	Cough and clear sputum	Bilateral pulmonary involvement	Large quantity clear frothy sputum, late stage
10. Jennings[59] 1948	58	W	F	10 mo.	Onset: dry cough; subsequently frequent colds and grad. incr. dyspnea. Later: cough, sputum, pleuritic pain, dyspnea, 10 lb. wt. loss; hemoptysis last 2 mo. of life	Mottling in both upper zones and opacities at bases with lat. fading. Patch of density in mid-zone of rt. lung, coarse mottling on left. Lower parts of lungs resembled confluent bronchopneumonia	Much purulent sputum. Later: more frothy profuse, still purulent. Hemoptysis later
11. Jennings[59] 1948	56	W	M	12 mo.	Chills, fever, left chest pain, cough, slight hemoptysis, left-sided pleurisy. 40 lb. wt. loss	Coarse patchy mottling all zones rt. lung with incr. vascular pattern. LUL clear, LLL opaque, medial zone of density	Purulent, slightly bloody
12. Drymalski, Thompson, and Sweany[30]* 1948	34	W (Polish)	F	About 14 mo.	On first adm: nonproductive cough, 4 lb. wt. loss. 9 mo. later: bronchopneumonia with fever (105°), hemoptysis, right lower chest pain	Routine x-ray few mo. prior to first adm: 3 cm. cavity in RLL. X-ray after penicillin during first adm: some clearing of the soft infiltrate about cavity wall. 6 mo. after first adm: no changes in comparison with prev. chest films. About 14 mo. from first x-ray (on second adm.): Consolidation and atelectasis of RLL	Initially nonproductive. Hemoptysis
13. Drymalski, Thompson, and Sweany[30]* 1948	55	W	F	6 mo.	4 mo. prior to adm: developed mild cough. On adm: cough, small amount sputum occasionally streaked by blood; fatigue, weakness. Later: became progressively more dyspneic and weaker	On adm: Areas of marked haziness in both lungs, most pronounced in the right. Cardiac shadow was displaced to left	Small amt: occasionally blood streaked. 1 mo. prior to death: positive for Ca

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Lobar adeno-carcinoma	Both lungs	None described	Symptomatic	Dead
Post-mortem	Pulmonary adenomatosis	All 5 lobes of lungs	None	Supportive	Dead
Post-mortem	Alveolar-cell tumor	All lobes of both lungs	Mediastinal nodes	Symptomatic	Dead
Post-mortem	Alveolar-cell tumor	Lower lobes, both lungs	None	Symptomatic	Dead
Resection	Pulmonary adenomatosis	Right lower lobe	None	First adm: 1 million units of penicillin. Second adm: lobectomy	"P.O. course uneventful." No follow-up
Papanicolaou (diag. pulm. Ca.). Needle biopsy (diag. Sq. cell Ca). Post-mortem	Pulmonary adenomatosis	Both lungs in mid-zones; nodule beneath pleura in rt. base	None seen (*lungs only* removed at post-mortem)	None recorded	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
14. Drymalski, Thompson, and Sweany[30]* 1948	45	W	F	22 mo.	2 yr. prior to adm.: influenza for 3 wk. Fatigue, intermittent cough, usually nonproductive; 25 lb. wt. loss, poor appetite, failing strength. After adm: progressive severe dyspnea. 2 mo. prior to adm: pulm. hemorrhage of 10 oz.	17 mo. before admission: "Evidence of a pulmonary lesion." Later: marked hazy infiltration of right lung and of middle field of left lung	2 mo. before adm: pulm. hemorrhage of 10 oz. No malig. cells found. Cough was usually nonproductive
15. McCallum[84] 1948	52	W	M	18 mo.	Cough, frothy sputum, weight loss. Later: dyspnea, cyanosis, pleuritic chest pain, slight fever	Initially: density in the lt. lung, more marked in upper and middle zones. 6 mo. later: patchy opacities throughout whole lt. lung field. 17 mo. later: lt. lung solid, spread to RUL	Cupful daily, thin, frothy. Hemoptysis on occasion
16. Shipman, Stephens, and Binkley[63] 1949	51	W	F	8 yr.	Cough and sputum	Area of incr. density, roughly triangular in shape, lying just above the diaphragm and posterior to lower portion of major fissure. Bronchograms showed bronchiectasis, right lower lobe	Originally small amt. of clear, frothy, glairy mucoid sputum. Later: increasing amount, thick, yellow, foul
17. Laipply and Fisher[32] 1949	51	W	F	3 mo.	Difficulty in breathing, cough, and weakness	Slight passive congestion of both lungs	Not recorded
18. Laipply and Fisher[32] 1949	45	W	M	10 mo.	Pain in chest and cough, 9 mo. Worse recently with hemoptysis, shortness of breath, increasing chest pain, anorexia	Diffuse mottling in lung fields due to small areas of incr. density in all lobes of both lungs, esp. central regions and lower lobes	Bloody
19. Hatfield and Hill[66] 1949	54	W	F	5 yr.	Dyspnea, cough, sputum, anorexia, fatigue, weight loss	Diffuse scattered nodular areas of incr. density, all areas both lungs. Films made 10 mo. previously showed large rounded oval area of incr. density, left base and scattered nodular areas, right base	Slight at first, later increased. Positive Papanicolaou
20. Freedman[23] 1949	29	W	F	9 mo.	Chest pain, cough, sputum, loss of weight, dyspnea	Bilateral disseminated nodular disease	Large quantities, thin, watery. Negative for AFB

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	Entire rt. lung; in lt. similar lesion fanned out from hilum and reached pleura lat. and base posteriorly.	None	Pneumothorax (discontinued after 1 yr.)	Dead
Post-mortem	Alveolar-cell tumor of lung	Entire left lung, right apex and superior segment, right lower lobe			
Resection	Pulmonary alveolar adenomatosis	Right lower lobe	None noted at operation	Right lower lobectomy	Living 9 mo. P.O. Areas of density in remaining right lung
Post-mortem	Primary alveolar-cell tumor	All lobes, both lungs	None	Symptomatic	Dead
Post-mortem	Primary alveolar-cell tumor	All lobes, both lungs	Pleura, intrapulmonary lymphatics, mediastinal and cervical nodes, left adrenal gland	Symptomatic	Dead
Papanicolaou	Pulmonary adenomatosis	All lobes, both lungs	Hilar nodes None	Symptomatic	Dead
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None	Treated for tuberculosis	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
21. Bubis and Erwin[6] 1949	66	W	M	3 mo.	Chest pain, intermittent fever, severe cough and yellow sputum	Linear basal markings incr. bilaterally with considerable pneumonitis in these areas. Slight amt. left pleural fluid. Bronchograms: bilateral basal bronchiectasis	Yellow, mucoid
22. Bubis and Erwin[6] 1949	63	W	M	5 yr.	Cough, shortness of breath	Patchy opacity throughout lower three-fourths of rt. lung; large areas of consolidation mid-portion of left; apparently many fibrous strands along line of bronchial trunks, lower half, lt. lung. Radiologist's imp: Granulomatous, probably fungus	Moderate amounts
23. Effert[85] 1949	68	W	F	8 yr.	Three episodes of pneumonia, 8, 7, and 6 yr., prior to death. Gradual downhill course with increasing dyspnea and cough. Overwhelming weakness 1 yr. prior to death	Innumerable, bilateral, rather symmetrical, somewhat confluent densities. Thought to represent massive hematogenous metastases from an unknown primary carcinoma	Amount and character not recorded
24. Liavaag[86] 1949	83	W	F	5 yr.	Angina pectoris and cardiac failure. Admitted to hospital with diagnosis of cardial infarcation. Tumor was in very early stage; no clinical symptoms	Not done	None
25. King and Carroll[51] 1950	63	N	F	1 yr.	Cough and sputum	Diffuse involvement, more marked on left	Amount and type not recorded
26. King and Carroll[51] 1950	58	W	F	5 yr. 3 mo.	Severe cough, mucoid sputum, severe dyspnea	Mar. 1945: Patchy incr. density base LUL. Feb. 1947: Patchy pneumonia, LLL June 1947: Patchy infiltrations, left Oct. 1948: Patchy consolidation, LLL. Thereafter serial films showed slow but progressive involvement of both lungs by confluent nodular densities. LLL had been removed in Nov. 1948 and scattered nodular densities of LUL and RLL were noted by Dec. 1948.	None early in disease; later copious, mucoid

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None	Sulfadiazine	Dead
Post-mortem	Pulmonary adenomatosis	Both lobes, left lung; upper and middle lobes, right lung	None	Symptomatic	Dead
Post-mortem	Primary diffuse alveolar epithelial carcinoma	"Diffuse, penny-sized lesions, more or less symmetrical in both lungs"	Hilar nodes, liver, paraaortic nodes, lymph nodes in porta hepatis	None	Dead
Post-mortem	Alveolar-cell tumor	Left upper lobe	None	None	Died second hosp. day (not due to tumor)
Needle biopsy	Pulmonary adenomatosis	All lobes, both lungs	None noted	Symptomatic	Dead
Resection	Pulmonary adenomatosis	Left lower lobe	None noted at operation (autopsy not permitted)	Resection, left lower lobe; later irradiation, finally symptomatic	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
27. King and Carroll[51] 1950	53	W	F	Less than 2 mo.	Shortness of breath, chest pain, generalized aches. Cough, copious sputum, anorexia, nausea, vomiting, weakness, weight loss	Innumerable soft nodular densities throughout both lungs. Nodules poorly outlined, more numerous in middle and lower lung fields where nodules became so confluent as to obscure the heart shadow	Thin, watery, frothy; as much as 1,000 c.c. in 24 hr.
28. Good, McDonald, Clagett, and Griffith[10] 1950	54	W	F	12 mo.	Severe nonproductive cough	Area of consolidation in left lower lobe	None
29. Good, McDonald, Clagett, and Griffith[10] 1950	34	W	F	7 mo.	Chronic cough, intermittent low-grade fever	Poorly circumscribed area, apparently pneumonitis, posterior to hilum in left lung	Meager, clear, whitish
30. Good, McDonald, Clagett, and Griffith[10] 1950	62	W	F	6 mo.	Nonproductive cough	Pleural reaction around left hemidiaphragm, large area of consolidation in left lower lobe	Almost none. Papanicolaou positive
31. Good, McDonald, Clagett, and Griffith[10] 1950	47	W	F	4 yr. (?)	Chronic cough, sputum occasionally blood tinged	Area of pneumonitis in left lower lobe	2 yr. before adm: severe prod. cough; bloody on 1 occ. On adm: clear, watery
32. Good, McDonald, Clagett, and Griffith[10] 1950	53	W	M	18 mo.	Chronic productive cough	Dense hemispherical mass in right chest occupying lower three-fourths of right hemithorax	Frothy white; blood on 1 occ. Papanicolaou negative
33. Good, McDonald, Clagett, and Griffith[10] 1950	30	W	F	1 yr.	Chronic productive cough	Dense irregular mass in left lower lobe; smaller irregular patch in right upper lobe opposite hilum	Gray mucoid, occasionally blood streaked. Positive Papanicolaou, probably alveolar-cell ca
34. Good, McDonald, Clagett, and Griffith[10] 1950	55	W	F	2 yr.	Chills, fever, cough with some blood	Area of pneumonitis in the lingula	Cough nonprod. until just before adm. when she raised some blood. Papanicolaou positive, thought to be of alv. cell type
35. Good, McDonald, Clagett, and Griffith[10] 1950	49	W	M	4 mo.	Chronic productive cough, 12 lb. wt. loss. Fever abated following penicillin	Elevation of lt. hemidiaphragm, fluid in rt. pleural space, poorly circumscribed mass in superior portion of RLL	½ cup daily, yellow. Papanicolaou positive
36. Good, McDonald, Clagett, and Griffith[10] 1950	57	W	M	6 mo.	Dyspnea and weakness on exertion, occasional nonproductive cough	"Generalized, diffuse tuberculosis of both lungs"	None

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None	Symptomatic	Dead
Resection	Alveolar-cell tumor	Left lower lobe	None	Resection, left lower lobe	Dead
Resection	Alveolar-cell tumor	Left lower lobe	None	Lobectomy, left lower lobe	Died of Hodgkin's dis. 2 yr. P.O.
Resection	Alveolar-cell tumor	Left lower lobe	None	Lobectomy, left lower lobe	Living 2 yr. P.O.
Resection	Alveolar-cell tumor	Left lower lobe	None	Lobectomy, left lower lobe	Good immed. result. Contact lost
Pneumonectomy	Alveolar-cell tumor	RML voluminous. Many nodules in upper and lower lobes	None at operation	Right pneumonectomy	Lesion in left lung 7 mo. later
Papanicolaou	Alveolar-cell tumor	Left lower lobe, right upper lobe, right lower lobe	None	Lobectomy, LLL. Lobectomy, RUL. Seg. resection, portion of RLL	Dead of rt. heart failure sixth P.O. day after second operation
Papanicolaou	Alveolar-cell tumor		None	Lobectomy, left upper lobe	Clinically well 6 mo. P.O.
Papanicolaou	Alveolar-cell tumor		None	Pneumonectomy, right	Well (recently op. uneventful P.O.)
Post-mortem	Alveolar-cell tumor	All lobes, both lungs	None	Symptomatic	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
37. Good, McDonald, Clagett, and Griffith[10] 1950	44	W	F	11 mo.	Productive cough and dyspnea on exertion	Large mass in left lower lobe, many nodules throughout both lungs	Watery, sometimes yellow, occasionally foul. Bloody on few occasions
38. Good, McDonald, Clagett, and Griffith[10] 1950	56	W	M	2 yr.	Chronic cough, dyspnea on exertion. Substernal pain for 3 mo.	Poorly defined mass in right lung. Many nodules scattered throughout both lungs	Occasional blood
39. Good, McDonald, Clagett, and Griffith[10] 1950	46	W	M	3½ mo.	Shortness of breath and weakness. Productive cough	Diffuse nodular lesions involving all lobes of both lungs, sparing only the apices and costophrenic angles	Character not recorded
40. Weir[15] 1950	63	N	F	1 yr.	Cough, copious sputum, night sweats, 20 lb. wt. loss	Conspicuous density in lower half of right lung field involving almost all of left	About "a quart" daily; clear, watery, frothy
41. Weir[15] 1950	58	W	F	44 mo.	Sweats, left subcostal pleuritic pain, cough and sputum, vomiting	Mar. 1947: density in lt. base resembling unresolved pneumonia. 1947: infiltration in left lower lung field interpreted as chronic pneumonitis. 1948: same	Purulent, later frothy. 207 c.c./day. None early in disease
42. Weir[15] 1950	53	W	F	7 wk.	Cough with copious sputum, weakness, anorexia, weight loss, nausea, vomiting	Miliary nodules throughout all lobes, both lungs, most dense at hilar regions	"Coffee can full" of watery, foamy sputum daily. Neg. for AFB
43. Davis and Simon[9] 1950	83	W	F	1 mo.	Shortness of breath, increasing fatigue, anorexia	Irregular conglomerated areas of increasing density involving the greater part of both lung fields	None
44. Davis and Simon[9] 1950	70	W	F	2 yr.	Chronic cough, profuse expectoration, 15 lb. wt. loss, irregular fever 1 mo. prior to adm.	Infiltrative process throughout both lungs with cyst formation in some areas. 1 wk. later: extension of pneumonia on both sides with considerable LLL by more chronic disease and considerable involvement of RUL by a new process.	Profuse. Negative for AFB
45. Davis and Simon[9] 1950	57	W	F	21 mo.	Right chest pain, dull. 5 lb. wt. loss. Later: constant hacking cough and increasing pleuritic chest pain	This was interpreted as lung cyst with infection. Infiltrative process in RML. Bronchography showed incomplete filling of bronchial tree in RML, other bronchi normally outlined. 6 wk. later: complete opacity of right lower chest	None when admitted. 6 wk. later: faint blood-streaked sputum

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Bronchial biopsy	Alveolar-cell tumor	All lobes, both lungs	Regional nodes and adrenals	Irradiation	Dead
Post-mortem	Alveolar-cell tumor	All lobes, both lungs	None	None	Sudden death 10 days after admission
Post-mortem	Alveolar-cell tumor	All lobes, both lungs	Hilar nodes and liver	None	Died 4 days after adm.
Pap. was suspicious. Aspiration biopsy positive. Conf. at post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None mentioned	Supportive	Dead
Resection	Pulmonary adenomatosis	Left lower lobe and lingula	Not stated	Lobectomy, left lower lobe	Ret'd. 5 mo. P.O. coughing incessantly. 1,183 c.c. sputum daily. Died shortly
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None mentioned	Symptomatic	Dead
Post-mortem	Alveolar-cell tumor	All lobes, both lungs	None	Symptomatic and supportive; penicillin	Dead
Post-mortem	Alveolar-cell tumor	All lobes, both lungs. Both lower lobes and about ⅓ of each upper lobe consolidated	None	Penicillin, aminophylline for pulmonary edema, digitalis	Dead
Lung biopsy	Alveolar-cell tumor	All lobes of right lung	Autopsy not done. Questionable visceral and parietal pleural metastasis	Penicillin and supportive	Died about 9 mo. after explor. thoracotomy

TABLE II

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
46. Davis and Simon[9] 1950	75	W	F	1 mo.	Productive cough and dyspnea. 15 lb. wt. loss (had been on reducing diet). Later: cyanotic, neck veins engorged, lethargic	Mottled infiltration throughout entire right lung and similar process in upper portion of left lung	Moderate amounts, white, foamy. No AFB on culture
47. Davis and Simon[9] 1950	78	W	F	2 yr.	Dyspnea 2 yr. Chest cold 2 mo. Severe dyspnea on adm., pain in left chest, ankle edema, engorgement of neck veins, cyanosis	Not done	Bloody on several occasions
48. Moyer[87] 1950	37	W	F	3 mo.	Cough, increasing malaise, dyspnea	Adm: increased lung markings, all lung fields. Flocculent, structureless density, rt. lower chest which obscured all lung markings. 1 mo. later: lesion in lt. base, similar to rt. Later spread to involve entire left lower lobe	Yellowish-white, frothy, small amount. Negative for AFB, fungi, etc
49. Gagné[68] 1950	37	W	M	14 mo.	Productive cough	Homogeneous opacity from rt. hilum to rt. base. 2 yr. later: rt. costophrenic sulcus had become obliterated and opacity had appeared at lt. hilum. 1 yr. later: most of both lung fields were involved	Character not recorded. Neg. for TBC. No Pap. until 2 yr. after lesion found; alv.-cell Ca. recognized
50. Paul and Juhl[69] 1950	48	W	F	9 mo.	Cough, copious sputum, chest pain, dyspnea, chronic fatigue	Marked density, basal half, lt. lung field. Mottled density in lt. mid-lung; upper ⅓ clear. On rt., homogeneous density, lower ⅓, upper lobe, patchy and stringy density from hilum along rt. cardiac border to the medial base. 8 mo. later: bilateral advance of disease	Copious, clear, watery
51. Paul and Juhl[69] 1950	67	W	M	4 mo.	Severe, persistent cough, copious sputum	Homogeneous density paralleling lt. cardiac border and extending from hilum down toward the base. 8 mo. P.O.: increase in homogeneous density bilaterally with almost complete consolidation of central and basal lt. lung field; similar findings involving all of right lung except upper ⅛	Original mucoid, later blood tinged. Terminal phase: "several pints" daily, clear, watery. Papanicolaou showed "abnormal cells"

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Alveolar-cell tumor	Both lungs, all lobes	None	Symptomatic and supportive	Dead
Post-mortem	Alveolar-cell tumor	Both lungs	None	Supportive	Dead 1 day after adm. Art. scl. heart dis. and cardiac failure
Post-mortem	Pulmonary alveolar adenomatosis	All lobes, both lungs	None	Symptomatic	Dead
Papanicolaou; post-mortem	Alveolar epithelioma of lungs, pulmonary pseudoadenomatosis	Bilaterally diffuse terminally. Right lower lobe initially	None	Symptomatic	Dead (about 3 yr. after adm.)
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None	None	Died during lung biopsy, 16 mo. after onset
Resection. Papanicolaou	Pulmonary adenomatosis	Originally left lower lobe. Later: all lobes both lungs	Pleural at least	Left lower lobectomy; no treatment of recurrence and/or spread	Moribund 4 mo. after adm. Probably dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
52. Paul and Juhl[69] 1950	42	W	M	Not stated	Severe productive cough; pain in left hip	Rounded mass of soft tissue density overlying upper mediastinum. Wedge-shaped areas of conglomerate density in both central and basal lung fields; triangular shadow on rt. at medial base. Bone destruction, left hip	6-8 ounces daily, tenacious, yellow
53. Paul and Juhl[69] 1950	42	W	M	2 mo.	Chronic, productive cough. 50 lb. wt. loss in 2 mo.	Homogeneous density obscuring middle ⅔ lt. lung field. Bronchography showed multiple cavities communicating with lingular bronchus. 6 mo. P.O.: widespread mottled density, right lung	Foamy, thick, yellow-white, no blood. On standing would separate into upper foamy and bottom watery layer. One pint daily
54. McCoy[52] 1951	60	W	M	14 mo.	Marked dyspnea; severe, paroxysmal coughing, productive	Deviation of tracheal and mediastinal shadow to rt.; diffuse, mottled infiltrate, bilateral, extending peripherally from the central lung fields. 14 mo. previously: numerous bilateral parenchymal deposits	Clear, thin, frothy
55. McCoy[52] 1951	31	W	F	1½ mo.	Dyspnea on exertion, mild nonproductive cough	1 wk. before adm: resembled miliary tuberculosis. Adm. films: diffuse mottling throughout both lungs most dense in the hilar areas and radiating well out into the periphery. Subsequent x-rays showed confluence of lesions	None. Papanicolaou positive, Class V
56. Peterson and Houghton[14] 1951	59	W	M	4 or 5 yr.	Increasing cough, marked fatigue	Lt. hemidiaphragm elevated, several circumscribed areas of infiltration in region of lingula, each measuring 1-2 cm. diameter	Hemoptysis once, productive cough
57. Peterson and Houghton[14] 1951	56	W	M	2½ yr.	Weight loss, cough	Poorly visualized rt. lung obscured by marked shift of mediastinum to rt.; generalized incr. density and atelectasis. Moderate infiltration in all parts of this lung and similar process apparent on the lt. with exception of the apex	Not stated

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	Right lung only	Pericardium, hilar nodes, liver, adrenals, sternum, ilium	X-ray to bone lesion, hip	Dead
Resection	Pulmonary adenomatosis	Originally left lung. P.O.: spread to entire right lung	None at operation	Pneumonectomy, left	Moribund from spread to entire right lung
Post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Liver, tracheobronchial nodes	Symptomatic	Dead
Papanicolaou	Alveolar-cell carcinoma	All lobes, both lungs	Hilar nodes, vertebral bone marrow	Nitrogen mustard without benefit	Died of respiratory insufficiency (36 days after adm.)
Resection	Pulmonary adenomatosis	Lingula	None	Segmental resection, lingula	No evidence of recurrence 28 mo. later
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	None described	Nitrogen mustard, streptomycin, no benefit	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
58. Gepts[75] 1951	72	W	F	2 mo.	Dyspnea, dry cough	Not described	None
59. Kent[49] 1951	40	W	M	4 yr.	Cough 4 yr. 2 mo. cough worse, sputum. Dyspnea, lassitude	Extensive patchy consolidation throughout rt. lung with patchy collapse, posterior basal segment, RLL. Appearance suggests an old inflammatory lesion with superadded bronchiectasis rather than carcinoma. Left lung normal	½ oz., mucoid, morning
60. Kent[49] 1951	54	W	M	8 mo.	Right pleural effusion, sterile and blood stained. Increasing dyspnea, cough with scanty sputum, 8 lb. wt. loss	Rt. pleural effusion, infiltration and cavitation rt. upper zone. Appearance that of tuberculosis, no radiologic evidence Ca	Scanty (bronchial aspirate neg. sterile)
61. Rosewood, Boucot, and Aegerter[88] 1951	16	?	M	3⅓ yr.	No symptoms (discovered on photofluorogram taken for pre-employment application)	3⅓ yr. preop: photofluorogram showed small rounded mass with central area of rarefaction at lt. base (LLL). 2⅓ yr. preop: x-ray revealed no change; 2 mo. preop: increase in size of lesion	None; negative P.P.D. test, first strength
62. Voluter and Rywlin[89] 1951	55	W	F	5 mo.	Symptoms of bronchitis with productive cough, asthenia, pallor, cachexia	Diffuse infiltration, right lower lobe. Emphysema; elevation, right hilum. Later: numerous nodules throughout all lobes, right lung, except extreme apex	Negative for AFB; Papanicolaou negative, pos. for Friedlander's
63. Bass and Singer[79] 1951	59	W	M	15 yr.	Cough and sputum for 15 yr. Adm.: severe cough, dyspnea, weakness	Dense homogeneous opacity of rt. hemithorax with retraction of trachea and mediastinum to rt. Bullous emphysema, lt. upper lung. Mottled infiltration, lower ⅓, lt. lung field. X-rays during past 15 yr. showed multiple cystic areas with fluid levels	Purulent; negative for AFB, Papanicolaou not done

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	All lobes, both lungs	Hilar and supraclavicular nodes, vertebral bodies	None	Dead
Resection	Alveolar-cell carcinoma	Right lung	None	Pneumonectomy, right	Died 24 hr. P.O. from pulmonary embolus
Post-mortem	Alveolar-cell carcinoma	RUL replaced by a gelatinous hemorrhagic mass	Supraclavicular nodes only, left	None	Dead
Resection	Solitary pulmonary adenoma (focal pulmonary adenomatosis)	Solitary tumor in LLL, near interlobar fissure directly beneath pleura	None	Local enucleation plus margin of lung tissue for biopsy	Alive and well 2¾ yr. P.O. No recurrence
Post-mortem	Primary unilateral alveolar cancer of the lung	RLL solidified and contained cavity. Nodules, RML and RUL	Liver, spleen, and abdominal nodes	Symptomatic	Died shortly after adm.
Post-mortem	Co-existing lobar adenocarcinoma and cystic disease of lung	Entire right lung	Mediastinal lymph nodes	Supportive	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
64. Abbott[50] 1951	67	N	M	1 mo.	Severe cough, weakness, weight loss, râles and rhonchi	X-ray diagnosis: mycotic infection	Minimal, mucoid; malignant cells seen
65. Abbott[50] 1951	60	W	F	6 wk.	Cough, weight loss, anorexia, dyspnea	X-ray diagnosis: lung abscess and bronchiectasis	Moderate, mucoid; Papanicolaou negative
66. Abbott[50] 1951	60	W	F	3 yr.	Cough, dyspnea, weakness, anorexia, weight loss, fever	X-ray diagnosis: diffuse lung tumor	None
67. Abbott[50] 1951	63	W	M	2 mo.	Cough, weakness, dizziness, blurring of vision, dyspnea, râles, dullness, friction rub over base of right lung	X-ray diagnosis: metastatic carcinoma or fungus infection	None
68. Abbott[50] 1951	44	W	M	2 yr.	Cough, much sputum, weakness, fever, leukocytosis, pain in chest; impaired resonance, moist râles, increased tactile fremitus	Not recorded	Copious, jelly-like
69. Kennamer[54] 1951	39	W	M	13 mo.	Weakness, dyspnea, large sputum production. Onset was with pleuritic pain, fever	Originally: lt. pleural effusion. Later: homogeneous density involving entire lt. hemithorax and lower ¾ of right	Blood streaked. On 1 occ. 3.3 L. in 12 hr. Usually 2-3 pints daily. Neg. for AFB
70. Watson and Smith[58†] 1951	62		M	9 mo.	Cough, chest pain	Multiple nodules	Not examined
71. Watson and Smith[58†] 1951	35		M	2 mo.	Chest pain	Mass filling chest	Not examined
72. Watson and Smith[58†] 1951	42		M	4 mo.	Dyspnea and dysphagia	Multiple nodules	Not examined
73. Watson and Smith[58] 1951	55		M	5 mo.	Cough	Hilar mass; peripheral nodule	Not examined
74. Watson and Smith[58†] 1951	61		F	2 mo.	Cough	Solitary nodule; pleural effusion	Negative for tuberculosis
75. Watson and Smith[58†] 1951	55		M	2 mo.	Loin pain	Hilar mass	Not examined
76. Watson and Smith[58†] 1951	59		M	6 wk.	Chest pain	Hilar mass	Negative for tuberculosis
77. Watson and Smith[58†] 1951	59		M	1 mo.	Dyspnea	Pleural effusion	Not examined
78. Watson and Smith[58†] 1951	48		M	6 mo.	Back pain	Hilar mass	Not examined
79. Watson and Smith[58†] 1951	41		F	6 mo.	Pneumonia	Solitary mass	Not examined

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Papanicolaou	Pulmonary adenomatosis and alveolar-cell carcinoma	Both lungs	Hilar nodes	None	Dead
Resection	Pulmonary adenomatosis and alveolar-cell carcinoma	Right upper and middle lobes	None	Pneumonectomy, right	Well 1 yr. P.O.
Post-mortem	Pulmonary adenomatosis and alveolar-cell carcinoma	Both lungs	Hilar nodes and pericardium	None recorded	Dead
Post-mortem	Pulmonary adenomatosis and alveolar-cell carcinoma	Both lungs	Hilar and aortic nodes, liver, and adrenal	None recorded	Dead
Post-mortem	Pulmonary adenomatosis and alveolar-cell carcinoma	Both lungs	None	None	Dead
Post-mortem	Pulmonary adenomatosis	Both lungs	None	Antibiotics and supportive	Dead
Post-mortem	Terminal bronchiolar carcinoma	Left lower lobe	Yes. Location not recorded. "Distant"	X-ray	Died 11 mo. after onset of symptoms
Post-mortem	Terminal bronchiolar carcinoma	Scattered foci, entire lt. lung	Yes. Location not recorded. "Distant"	Symptomatic	Dead
Biopsy of skin nodule; post-mortem	Terminal bronchiolar carcinoma	Right lower lobe	Yes. Location not recorded. "Distant"	Symptomatic	Dead
Cervical lymph node biopsy	Terminal bronchiolar carcinoma	Left upper lobe	Yes. Location not recorded. "Distant"	X-ray	Dead
Post-mortem	Terminal bronchiolar carcinoma	Right middle lobe	Hilar nodes	X-ray	Dead
Post-mortem	Terminal bronchiolar carcinoma	Left upper lobe	Hilar nodes and "distant"	X-ray	Dead
Thoracotomy; aspiration biopsy	Terminal bronchiolar carcinoma	Left lower lobe	None	Pneumonectomy	Died 19 mo. P.O.
Post-mortem	Terminal bronchiolar carcinoma	Entire left lung	Yes. Location not recorded. "Distant"	Symptomatic	Dead
Post-mortem	Terminal bronchiolar carcinoma	Right hilar area	Yes "distant" (bone)	X-ray to bone	Died 11 mo. after onset of symptoms
Thoracotomy	Terminal bronchiolar carcinoma	Right lower lobe	None	Lobectomy	Alive and well after 5 yr.

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
80. Watson and Smith[58†] 1951	50		M	—	None	Infiltrative mass	Not examined
81. Watson and Smith[58†] 1951	51		M	5 mo.	Pneumonia	Multiple nodules	Not examined
82. Watson and Smith[58†] 1951	28		M	6 mo.	Shoulder pain	Mediastinal mass	Not examined
83. Watson and Smith[58†] 1951	57		F	10 mo.	Pain, cervical spine	Pleural effusion	Not examined
84. Watson and Smith[58†] 1951	39		M	4 mo.	Chest pain	Mediastinal mass	Papanicolaou Class III
85. Watson and Smith[58†] 1951	62		M	1 mo.	Chest pain	Solitary mass	Papanicolaou Class V
86. Watson and Smith[58†] 1951	58		F	1 mo.	Chest pain, wheezing	Solitary mass	Papanicolaou Class V
87. Watson and Smith[58†] 1951	50		M	3 mo.	Virus pneumonia	Multiple nodules	Papanicolaou Class V
88. Watson and Smith[58†] 1951	59		M	1 yr.	Dyspnea	Patchy density	Papanicolaou Class V
89. Watson and Smith[58†] 1951	59		M	—	None	Solitary mass	Not examined
90. Watson and Smith[58†] 1951	43		F	—	None	Solitary mass	Not examined
91. Watson and Smith[58] 1951	57		M	3 mo.	Chest pain	Pleural effusion	Papanicolaou Class I, negative for TBC
92. Watson and Smith[58] 1951	51		M	5 mo.	Chest pain	Pleural effusion	Not examined
93. Watson and Smith[58] 1951	51		M	6 mo.	Cough	Hilar mass; patchy density	Papanicolaou Class V
94. Watson and Smith[58] 1951	66		M	9 mo.	Cough	Hilar mass; atelectasis	Papanicolaou Class II
95. Watson and Smith[58] 1951	50		M	5 mo.	Dyspnea	Solitary mass	Papanicolaou Class III
96. Watson and Smith[58] 1951	52		F	?	Dyspnea	Solitary mass	Papanicolaou Class III
97. Watson and Smith[58] 1951	62		M	1 mo.	Chest pain	Infiltrative mass	Papanicolaou Class I
98. Watson and Smith[58] 1951	55		F	—	None	Solitary mass	Papanicolaou Class IV
99. Watson and Smith[58] 1951	41		M	1 yr.	Cough	Hilar mass	Papanicolaou Class IV
100. Watson and Smith[58] 1951	71		M	3 mo.	Chest pain	Multiple nodules	Papanicolaou Class IV
101. Watson and Smith[58] 1951	56		M	1 mo.	Cough, chest pain	Multiple nodules; bilateral	Papanicolaou Class IV

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Resection	Terminal bronchiolar carcinoma	Left upper lobe	None	"V" excision tumor	Alive and well after 5 yr.
Post-mortem	Terminal bronchiolar carcinoma	Right and left lungs	Yes; location not recorded "distant"	Symptomatic	Died 6 mo. after onset of symptoms
Post-mortem	Terminal bronchiolar carcinoma	Left upper lobe	Yes; location not recorded "distant"	X-ray to metastasis	Died 16 mo. later
Post-mortem	Terminal bronchiolar carcinoma	Left upper lobe	Yes; location not recorded "distant"	Symptomatic	Died 15 mo. later
Thoracotomy; post-mortem	Terminal bronchiolar carcinoma	Right upper lobe	Hilar nodes	Thoracotomy; inoperable	Died 6 mo. later
Papanicolaou	Terminal bronchiolar carcinoma	Right upper lobe	None	Pneumonectomy	Alive and well 26 mo. P.O.
Papanicolaou	Terminal bronchiolar carcinoma	Left upper lobe	Hilar nodes	Pneumonectomy	Died 9 mo. P.O.
Papanicolaou	Terminal bronchiolar carcinoma	Right lower lobe	Hilar nodes	Pneumonectomy	Died 6 mo. P.O.
Papanicolaou	Terminal bronchiolar carcinoma	Left lower lobe	Hilar nodes and "distant"	Symptomatic	Died 12 mo. later
Aspiration biopsy	Terminal bronchiolar carcinoma	Right lower lobe	Hilar nodes	Segmental resection and radiation	Alive 8 mo. P.O. with dis.
Resection	Terminal bronchiolar carcinoma	Left upper lobe	Hilar nodes	Pneumonectomy	Alive and well 8 mo. P.O.
Resection	Terminal bronchiolar carcinoma	Entire left lung	Hilar nodes	Pneumonectomy	Died 4 days P.O.
Lung (pleural) biopsy	Terminal bronchiolar carcinoma	Entire left lung	Hilar nodes and "distant"	X-ray	Alive 7 mo.
Papanicolaou	Terminal bronchiolar carcinoma	Right hilar area	Hilar nodes	Pneumonectomy	Alive 5 mo. P.O.
Biopsy supraclavicular node	Terminal bronchiolar carcinoma	Right upper lobe	Yes "distant"	X-ray	Alive 3 mo. after treat.
Resection	Terminal bronchiolar carcinoma	Left upper lobe	None	Lobectomy	Alive 2 mo. P.O.
Aspiration biopsy	Terminal bronchiolar carcinoma	Right upper lobe	None	Pneumonectomy	Alive 6 mo. P.O.
Supraclavicular lymph node biopsy	Terminal bronchiolar carcinoma	Left lung	Yes "distant"	X-ray	Died 5 mo. after treat.
Papanicolaou	Terminal bronchiolar carcinoma	Right upper lobe	None	Pneumonectomy	Alive 3 mo. P.O.
Papanicolaou	Terminal bronchiolar carcinoma	Right hilar area	Hilar nodes	Thoracotomy; x-ray	Alive 3 mo.
Papanicolaou	Terminal bronchiolar carcinoma	Diffuse, both lungs	Yes "distant"	Symptomatic	Died 4 mo. later
Papanicolaou	Terminal bronchiolar carcinoma	Diffuse, both lungs	Yes "distant"	X-ray	Alive 3 mo. later

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
102. Watson and Smith[58] 1951	49		F	—	None	Solitary mass	Papanicolaou Class III
103. Kern, Lewinsky and Curran[55] 1952	65	W	M		Cough, fantastic amounts of sputum	Bilateral mottled densities in lower portions of both lungs and a confluent density massive, LLL. Mottled and confluent densities in lower ⅓ of rt. lung and lower ½ of left lung	Huge quantities, clear, frothy, mucoid. Strongly suspicious of pulmonary adenomatosis
104. Dennis, Raby, and Hildenbrand[28] 1952	51	W	M	8 mo.	Productive cough, shortness of breath, 30 lb. wt. loss; weak and emaciated, respirations loud and gurgling; had had chills and fever	Initially: homogeneous infiltration in periphery of RUL and in lt. base. 7 mo. later: Homogeneous consolidation of entire RUL, partial consolidation of rt. middle and lower lobes and the LUL	On adm: frothy, yellow resembling pale soapsuds
105. White, Madding, and Hershberger[62] 1952	34	W	M	Probably 11 yr.	Productive cough, wt. loss of 35-40 lb. in one yr.	7 yr. preop: unresolved pneumonia, RLL. 4 yr. preop: RLL lesions had become more extensive. 1 yr. preop: disease more extensive in rt. chest and entire lt. lower lung field was involved. Time of op: Consolidation of rt. lower lung field and probable pneumonic process, LLL. 3 yr. P.O. The pulmonary process had become more extensive	Copious, thick, frothy, mucopurulent, streaked with blood
106. Valentine and Wynn-Williams[29] 1952	41	W	F	About 1 yr.	Lt.-sided pleurisy 15 yr. previously; lt.-sided pneumonia on at least 4 occ. Cough, fever, sputum, dyspnea on exertion about 1 yr. 5 mo. after adm.: wt. had fallen 13 lb.; cough very troublesome. 8 mo. after adm: clubbing of fingers noted. 9 mo. severe dyspnea and pyrexia. 11 mo.: severe dyspnea, cyanosis, cough and frothy sputum	Extensive shadowing over the rt. lung, most marked in middle zone but also extending into the lower and slightly into the upper zones. The whole lt. lung field was opaque but in the upper and middle zones there were radiolucent areas of the type seen in cystic bronchiectasis. These shadows were seen to be an extension of those noted in films made 1 yr. prior to adm. 5 mo. after adm: extension of shadows on rt.	1-2 oz., frothy; bloody on several occasions

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Resection	Terminal bronchiolar carcinoma	Right upper lobe	None	Lobectomy	Alive 3 mo. without disease
Suspicious Papanicolaou. Needle biopsy	Pulmonary adenomatosis	Lower portions, both lungs	Not recorded	Irradiation with no diminution. Later nitrogen mustard with no apparent benefit	Present status unknown, probably dead
Post-mortem	Pulmonary adenomatosis	All lobes on right. Left upper lobe	Not recorded	Symptomatic	Died of respiratory insufficiency
Resection	Alveolar-cell tumor of the lung	RML at operation. At post-mortem entire remaining right lung; about ½ of left upper lobe	Right cerebral hemisphere, 2 tracheobronchial nodes, 1 periaortic node, liver	RML lobectomy, followed by irradiation. Symptomatic treatment only for spread and recurrence 4 yr. later	Good palliation after lobectomy, 2½ yr. Then recurrence and death
Post-mortem	Pulmonary adenomatosis	Right lung	None	Symptomatic	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
107. Valentine and Wynn-Williams[29] 1952	73	W	F	9 mo.	Increasing dyspnea, slightly productive cough	Dense shadowing over the lower and middle zones of the rt. lung, also slight mottling in the upper zone; some rounded densities in the upper and middle zones of lt. lung	Small amount, blood tinged
108. Valentine and Wynn-Williams[29] 1952	80	W	M	"Several" mo.	Shortness of breath on exertion, marked weight loss, progressive weakness: cough and sputum for 1 mo.	Slightly raised right hemidiaphragm, obscured costophrenic angle. Interlobar septum slightly thickened, moderate opacity of the middle zone, spreading slightly above and below it	Amount and character not noted
109. Dunham and Smith[70] 1952	64	W	M	2 mo.	Dyspnea, orthopnea, chronic cough and hemoptysis, 2 wk. Progressive weakness and fatigability for 2 mo. Occasional chest pain	Widespread diffuse nodular lesions bilaterally with confluence in left midlung and right base	Pink tinged; Papanicolaou positive
110. Hutchinson[19] 1952	36	?	F	6 mo.	Easily tired, frequent cough, expectoration for 6 mo. At 5 mo. prior to adm: pneumonia for 1 mo.; never fully recovered; thereafter chest pain persisted. On adm: dyspneic even at rest, frequent cough	Ill-defined opacity in lower part of rt. lobe with some faintly defined nodular opacities in upper part of rt. lobe; RUL and other lung appeared normal. 3 mo. P.O.: X-ray evidence of involvement of both the remaining portions of rt. and left lungs	Strikingly large quantities; white, frothy (clear watery layer on standing)
111. Hutchinson[19] 1952	38	?	M	4-5 mo.	Persistent cough for 4-5 mo.; loss of weight, breathlessness, 2 mo.; sputum worse during this period. Blood-stained sputum for 10 days prior to adm. On adm: severe dyspnea and short hacking paroxysmal cough; emaciated and cachectic	Diffuse mottling of both lungs, more on left than right. Diagnosis: TBC?, tumor?	"Worse" during 2 mo. before admission. Blood stained for 10 days prior to admission

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Pulmonary adenomatosis	Both lungs	None	Symptomatic	Dead
Post-mortem	Pulmonary adenomatosis	Both lungs	Mediastinal and cervical nodes	None	Dead
Papanicolaou	Terminal bronchiolar or "alveolar-cell" carcinoma of lung	All lobes, both lungs	Hilar and paratracheal nodes	Symptomatic	Died on 13th hospital day
Resection	Pulmonary adenomatosis	Right lower lobe	None	Right lower lobe lobectomy	Died at home 6 mo. P.O.
Post-mortem	Alveolar-cell carcinoma	Both lungs. LUL completely consolidated (probably primary here)	Extensive lymphatic involvement. Glands at hilum, lymphatic involvement along aorta into abdomen; surface of heart; right lobe of liver, kidneys, spleen	None recorded	Pt. gradually weaker, more dyspneic, pulse failed. Dead 22 days after adm.

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
112. Tillett and Hirsch[74]* 1952	57	W	M	15 yr. ?	Chronic, nonprod. cough for 15 yr.; worse past 5 mo. 6 wk. prior to adm: cold with mod. severe cough productive of yellow green phlegm. Anorexia for past 4 wk. 10 lb. wt. loss. Several days before admission: dyspneic with fever of 101° F.	Widespread infiltration of lung fields with a maximum involvement of the right upper lobe	6 wk. before admission: yellow-green phlegm
113. Tillett and Hirsch[74]* 1952	57	W	M	3-4 mo.	3-4 mo. prior to adm: became dyspneic. About 1 mo. later: cough when lying down, productive of about a tablespoon of brown sputum daily (about 3 yr. before had a pneumonia which cleared uneventfully)	Atelectasis of right upper lobe and some involvement of the middle lobe	2-3 mo. before adm: about a tablespoon of brown sputum daily
114. Tillett and Hirsch[74]* 1952	52	W	M	18 mo. ?	2 yr. before adm.: pleurisy of left chest. 1 yr. later: recurrence of this from which he never fully recovered. Gradually increasing shortness of breath for 18 mo. Occasional cough productive of copious white, frothy sputum which for 1 wk. had been streaked with blood. During 1 mo. before admission: almost constant chest pain	X-rays of G.I. tract were negative. X-ray of chest not recorded	"Copious," white, frothy. Streaked with blood for 1 wk. prior to adm.
115. Fisher and Holley[90]*	80	W	F	About 2 mo.	Dyspnea, chest pain, considerable weight loss. Later: became more emaciated and weaker quite rapidly	Large quantity of fluid in right pleural space. Fairly extensive fibrosis in right upper lobe. No lesions seen in left lung	Not mentioned

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	So-called pulmonary adenomatosis	Both lungs	None distant. (Blood vessels at periphery of lung, tracheobronchial lymph node.) Also intimal edge of branch of pulmonary artery	None recorded	Died on 5th hospital day
Resection	Papillary carcinoma of the lung (so-called pulmonary adenomatosis)	Right upper lobe, right middle lobe	None by clinical evidence (necropsy not done). Tumor cells found in blood vessels	Right pneumonectomy	Died outside of hosp.
Lung biopsy (bronchoscopy); resection	So-called pulmonary adenomatosis	Left lung	None recorded (necropsy not done)	Left pneumonectomy	Died outside of hosp.
Thoracentesis; post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Visceral and parietal pleura on rt.; visceral pleura on lt; diaphragm, hilar nodes (autopsy limited to thorax)	None recorded	Dead

TABLE II.

AUTHOR AND DATE	AGE	RACE	SEX	DURATION	SYMPTOMS	ROENTGENOGRAPHIC FINDINGS	SPUTUM
116. Fisher and Holley[90]* 1953	47	Y	M	Less than 3 mo.	On adm.: cough, expectoration, lower left chest pain. Later: left shoulder pain. Hospital course: progressively downhill with dyspnea, cyanosis, fever, wheezing respirations, weakness, weight loss	Innumerable stippled areas of increasing density in both lung fields. Suggested diagnosis: miliary T.B., pulmonary mycosis, and metastatic Ca (most probable)	Present but not described. Negative for TBC.
117. Fisher and Holley[90]* 1953	61	W	M	About 1 mo.	For 1 mo.: dyspnea, wheezing respirations, productive cough. Hospital course: became very weak and deteriorated rapidly	Diffuse mottling of both lung fields (suggestive of miliary T.B. but more probable diagnosis was pulmonary mycosis)	Present but amount not described. No hemoptysis
118. Fisher and Holley[90]* 1953	54	W	F	About 10 mo.	About 8½ mo. prior to adm.: "chest cold," dyspnea on exertion. About 7½ mo. prior to admission: "bronchitis." On adm.: increasing dyspnea, unproductive cough made worse by lying down	Widespread, rather fine mottling of both lung fields. Suggested diagnosis: pulmonary adenomatosis	None
119. Fisher and Holley[90]* 1953	62	W	M	About 3 mo.	Weakness, chest pain, wheezing and cough with scanty sputum. On admission: weight loss, slight fever. Later: weakness and dyspnea progressively worse	5 mo. prior to onset of symptoms: films during chest survey passed as within normal limits. On adm.: scattered, densely mottled infiltration throughout both lung fields; provisional diagnosis: miliary T.B. 1 mo. after adm.: bilateral extension of disease; diag. considered: fungus infection of lungs, miliary T.B., and carcinomatosis (most likely)	Scanty
120. Delarue and Graham[40]* 1949‡	35	W	M	8-12 mo.	Chronic productive cough. Some dyspnea on exertion with palpitation and vertigo	Infiltrative process in the right lower lung field	½ cup of foul-smelling greenish-yellow sputum daily. Small hemoptysis on 1 occasion

*Case not included in the statistical analyses on which the graphs are based.

†Although not so indicated in the report of Watson and Smith[58] these cases were previously reported by Smith, Knudtson, and Watson[57] in 1949.

‡Not listed in proper chronologic order through an oversight.

—CONT'D

METHOD OF DIAGNOSIS	AUTHOR'S DIAGNOSIS	LOCATION OF LESIONS	METASTASES	TREATMENT	RESULT
Post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Hilar, mediastinal and abdominal lymph nodes; liver, left kidney, adrenals, ribs and vertebrae	None recorded	Dead
Post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Hilar and mediastinal lymph nodes, pericardium, eighth left rib, liver, spleen	None recorded	Dead
Post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Hilar lymph nodes of both lungs	None recorded	Dead
Post-mortem	Alveolar-cell carcinoma	All lobes, both lungs	Hilar lymph nodes of both lungs, pericardium, sternum	None recorded	Dead
Resection	Alveolar-cell carcinoma of lung	Right lower lobe	None	Right lower lobectomy	Recurrence 3 yr. later with involv. of remaining portion of rt. lung and chest wall. Pneumonectomy

CONCLUSIONS

So-called benign pulmonary adenomatosis and malignant terminal bronchiolar or alveolar-cell carcinoma are one and the same condition, varying only in their degree of malignancy in different patients or in separate portions of the same tumor. The precise site of origin has not been definitely determined. The best evidence appears to indicate that they begin in the terminal bronchioles. They clearly arise in the periphery of the lung and whether it is from the alveoli or the bronchioles is clinically unimportant. Although many authorities have expressed the opinion that this disease is of multicentric origin, no convincing evidence to substantiate that opinion could be found. On the contrary, the established facts appear to indicate that the lesion begins in a single focus from which it may spread by local extension, lymphatic or blood-borne metastases, or bronchiogenic dissemination.

There are no distinctive clinical or radiographic features by which these tumors may be definitely recognized. In general, early symptoms are minimal or absent and the late complaints are those of any widespread chronic pulmonary disease. Certain characteristics, sometimes said to be typical of this disease, such as diffuse nodular lesions involving all five lobes of the lungs and the expectoration of huge quantities of glairy mucoid sputum, are late manifestations, seen principally in patients whose prognosis is hopeless. Among the various diagnostic methods which have been employed in the recognition of these tumors, only cytologic study of the sputum and histologic examination of the excised lesion have proved to be of real value. Search of the sputum stained by the Papanicolaou method has proved most rewarding and merits widespread use in the study of patients in whom this disease may be suspected.

Excisional surgery is the only hopeful treatment. In view of the peculiar growth characteristics and manner of spread of this neoplasm, conservative pulmonary resection would seem to be the treatment of choice in a majority of patients. Surgical treatment of patients with bronchiolar carcinoma was begun so recently that sufficient time has not elapsed to permit the accumulation of a large series of patients for five-year follow-up. There are indications, however, that with early resection the five-year survival rate in this group may be better than with any other lung cancer.

REFERENCES

1. Moritz, A. R.: The Pathologist's Approach to Pulmonary Neoplasms, Radiology **55**. 712, 1950.
2. Alexander, C. M., and Chu, F.: Pulmonary Adenomatosis Complicated by Lobar Pneumonia, Arch. Path. **43**: 92, 1947.
3. Dacie, J. V., and Hoyle, C.: Malignant Adenomatosis, "Alveolar Cell Tumor" of the Lung, Brit. J. Tuberc. **36**: 158, 1942.
4. Holman, W. L., and Duff, G. L.: Primary Carcinoma of the Lung, Am. J. M. Sc. **196**: 436, 1938.
5. Gordon, A. K.: Note on a Case of Primary Diffuse Alveolar Carcinoma of the Lung, Lancet **2**: 501, 1920.
6. Bubis, S., and Erwin, J. H.: Pulmonary Adenomatosis, Am. J. Med. **7**: 336, 1949.
7. Wenger, F.: Alveolar Cell Tumor, Case, Prensa méd. argent. **32**: 44, 1945.

8. Liebow, A. A.: Tumors of the Lower Respiratory Tract: Atlas of Tumor Pathology, Section V, Fascicle 17, p. 53, Washington Armed Forces Institute of Pathology, c1952.
9. Davis, M. W., and Simon, T. R.: Alveolar Cell Tumor of the Lung, Am. Rev. Tuberc. **62**: 594, 1950.
10. Good, C. A., MacDonald, J. R., Clagett, O. T., and Griffith, E. R.: Alveolar Cell Tumors of the Lung, Am. J. Roentgenol. **64**: 1, 1950.
11. Ikeda, K.: Alveolar Cell Carcinoma of the Lung, Am. J. Clin. Path. **15**: 50, 1945.
12. Geever, E. F., Carter, H. R., Neubuerger, K. T., and Schmidt, E. A.: Roentgenologic and Pathologic Aspects of Pulmonary Tumors Probably Alveolar in Origin, Radiology **44**: 319, 1945.
13. Swan, L. L.: Pulmonary Adenomatosis of Man; A Review of the Literature and Report of Nine Cases, Arch. Path. **47**: 517, 1949.
14. Peterson, E. W., and Houghton, J. D.: Pulmonary Adenomatosis, Report of Two Cases, New England J. Med. **244**: 429, 1951.
15. Weir, A. B., Jr.: Pulmonary Adenomatosis; Clinical Review and Report of Three Cases, Arch. Int. Med. **85**: 806, 1950.
16. Paul, L. W., and Ritchie, G.: Pulmonary Adenomatosis, Radiology **47**: 334, 1946.
17. Neubuerger, K. T., and Geever, E. S.: Alveolar Cell Tumor of the Human Lung, Arch. Path. **33**: 551, 1942.
18. Herbut, P. A.: Bronchiolar Origin of "Alveolar Cell Tumor" of the Lung, Am. J. Path. **20**: 911, 1944; Alveolar Cell Tumor of the Lung, Arch. Path. **41**: 175, 1946.
19. Hutchison, H. E.: Pulmonary Adenomatosis and Alveolar Cell Carcinoma, Cancer **5**: 884, 1952.
20. Silverman, G., and Angrist, A.: Lobar Adenocarcinoma of the Lung Simulating Pneumonia; Report of Two Cases, Arch. Int. Med. **81**: 369, 1948.
21. Weller, C. V.: The Pathology of Primary Carcinoma of the Lung, Arch. Surg. **7**: 478, 1929.
22. Decker, H. R.: Discussion of Stephens, H. B., and Shipman, S. J.: Pulmonary Alveolar Adenomatosis, Cancerous Pulmonary Adenomatosis, Alveolar-Cell Carcinoma of the Lung, Jaagsiekte? J. THORACIC SURG. **19**: 589, disc. 599, 1950.
23. Freedman, B.: Pulmonary Adenomatosis; Report of a Case, Am. Rev. Tuberc. **60**: 258, 1949.
24. Malassez, L.: Histological Examination of a Case of Encephaloid Cancer of the Lung (Epithelioma), Arch. de physiol. norm. et path., Par. **3**: 353, 1876.
25. Oppenheimer, J. M.: Non-Specificity of Germ Layers, Quart. Rev. Biol. **15**: 1, 1940.
26. Brachet, A.: Treatise on Embryology of Vertebrates, ed. 2, revised by Dalcq and Gerard, Paris, 1935, Masson & Cie. (Quoted by Oppenheimer.[25])
27. Waddell, W. R.: Organoid Differentiation of the Fetal Lung. A Histologic Study of the Differentiation of Mammalian Fetal Lung in Utero and in Transplants, Arch. Path. **47**: 227, 1949.
28. Dennis, J. M., Raby, W. T., and Hildenbrand, E. J. C.: Pulmonary Adenomatosis, Ann. Int. Med. **36**: 667, 1952.
29. Valentine, J. C., and Wynn-Williams, N.: Pulmonary Adenomatosis, Brit. J. Tuberc. **46**: 37, 1952.
30. Drymalski, G. W., Thompson, R., and Sweany, H. C.: Pulmonary Adenomatosis; A Report of Three Cases, Am. J. Path. **24**: 1083, 1943.
31. Wood, D. A., and Pierson, P. H.: Pulmonary Alveolar Adenomatosis in Man. Is This the Same Disease as Jaagsiekte in Sheep? Am. Rev. Tuberc. **51**: 205, 1945.
32. Laipply, T. C., and Fisher, C. I.: Primary Alveolar Cell Tumors of the Lung, Arch. Path. **48**: 107, 1949.
33. Simms, J. L.: Multiple Bilateral Pulmonary Adenomatosis in Man, Arch. Int. Med. **71**: 403, 1943.
34. Stewart, F.: Personal communication to Liebow.[8]
35. Fried, B. M.: Primary Carcinoma of the Lung, Arch. Int. Med. **35**: 1, 1925; Primary Carcinoma of the Lung, Bronchogenic Cancer—A Clinical and Pathologic Study, Am. J. Med. **10**: 373, 1931.
36. Adler, I.: Primary Malignant Growths of the Lungs and Bronchi; A Pathologic and Clinical Study, New York, 1912, Longmans, Green & Co.
37. Bell, E. T.: Hyperplasia of the Pulmonary Alveolar Epithelium in Disease, Am. J. Path. **19**: 901, 1943.
38. Ham, A. W., and Baldwin, K. W.: A Histological Study of the Development of the Lung With Particular Reference to the Nature of Alveoli, Anat. Rec. **81**: 363, 1941.
39. Macklin, C. C.: Alveolar Pores and Their Significance in the Human Lung, Arch. Path. **21**: 202, 1936; Residual Epithelial Cells on the Pulmonary Alveolar Walls of Mammals, Tr. Roy. Soc. Canad. Inst. **40**: 93, 1946.

40. Delarue, N. C., and Graham, E. A.: Alveolar-Cell Carcinoma of the Lung (Pulmonary Adenomatosis, Jaagsiekte?); A Multicentric Tumor of Epithelial Origin, J. THORACIC SURG. **18**: 237, 1949.
41. Smith, L. W., and Gault, E. S.: Essentials of Pathology, ed. 3, Philadelphia, 1948, The Blakiston Company.
42. Simon, M. A.: So-Called Pulmonary Adenomatosis and Alveolar Cell Tumors; Report of a Case, Am. J. Path. **23**: 413, 1947; Diffuse Primary Alveolar Carcinoma of the Lung (So-Called "Alveolar Cell" Tumor of the Lung), Am. J. Clin. Path. **17**: 783, 1947; Hamartomas of the Lung and So-Called "Pulmonary Adenomatosis," Am. J. M. Sc. **216**: 333, 1948.
43. Sweany, H. C.: A So-Called Alveolar Cell Cancer of the Lung, Arch. Path. **19**: 203, 1935.
44. Bliss, T. L.: Bronchorrhea, Its Occurrence in a Case of Bronchogenic Carcinoma, J. THORACIC SURG. **6**: 660, 1936.
45. Casilli, A. R., and White, H. J.: Rare Forms of Primary Malignant Lung Tumors, Am. J. Clin. Path. **10**: 623, 1940.
46. Aynaud, M., Peyron, A., and Falchetti, E.: On Cancer of the Lung in Sheep and Etiologic Comparisons with Parasitic and Infectious Lesions, Compt. rend. Acad. d. sc. **195**: 342, 1932.
47. Dungal, N., Gislason, G., and Taylor, E. L.: Epizootic Adenomatosis in the Lungs of Sheep—Comparisons with Jaagsiekte, Verminous Pneumonia and Progressive Pneumonia, J. Comp. Path. & Therap. **51**: 46, 1948.
48. Campbell, J. A.: Effects of Road Dust "Freed" from Tar Products Upon Incidence of Primary Lung Tumours of Mice, Brit. J. Exper. Path. **18**: 215, 1937.
49. Kent, J. V.: Primary Alveolar Cell Carcinoma of the Lung, Brit. J. Radiol. **24**: 216, 1951.
50. Abbott, J. E.: Pulmonary Adenomatosis and Alveolar Cell Carcinoma, Texas State J. Med. **47**: 826, 1951.
51. King, J. C., and Carroll, D. S.: Pulmonary Adenomatosis; A Report of Four Cases, Radiology **55**: 669, 1950.
52. McCoy, H. I.: "Alveolar-Cell" Carcinoma of the Lung, Ann. Int. Med. **34**: 968, 1951.
53. Fox, R. T.: Discussion of Stephens and Shipman.[22]
54. Kennamer, R.: Pulmonary Adenomatosis; Report of a Case, J. A. M. A. **145**: 815, 1951.
55. Kern, R. A., Lewinsky, W. J., and Curran, R. A.: Fluid, Electrolyte and Protein Depletion Secondary to Bronchorrhea of Pulmonary Adenomatosis—A Complication Heretofore Unreported, Am. J. M. Sc. **223**: 512, 1952.
56. Rey, J. C., and Rubinstein, P.: Gelatinous Cancer of the Lung in Bronchorrheal Form, Prensa méd. argent. **34**: 575, 1947.
57. Wood, E. H., Jr.: Unusual Case of Carcinoma of Both Lungs Associated With Lipoid Pneumonia, Radiology **40**: 193, 1943.
58. Watson, W. L., and Smith, R. R.: Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung; Report of 33 Cases, J. A. M. A. **147**: 7, 1951.
59. Jennings, G. H.: Lung Alveolar Tumors; A Report of Two Cases, Thorax **3**: 174, 1948.
60. Skorpil, F.: Pathology and Histology of Alveolar Epithelial Carcinoma; Case with Atypical Metastases into Lymph Nodes, Frankfurt, Ztschr. f. Path. **55**: 347, 1941; Pathology and Histology of Alveolar Epithelial Carcinoma, Zentralbl. allg. Path. **80**: 91, 1942-43.
61. Fernandez Luna, D., and Bracco, A. N.: Pseudopneumonic Pulmonary Cancer (Ewing's Diffuse Alveolar Cancer), Bol. An. Soc. tisiol. d. Hosp. nac. central, pp. 98, 1943.
62. White, J. N., Madding, G. F., and Hershberger, L. R.: Alveolar Cell Tumor of the Lung, Dis. Chest **21**: 655, 1952.
63. Shipman, S. J., Stephens, H. J., and Binkley, F. M.: Pulmonary Alveolar Adenomatosis, Am. Rev. Tuberc. **60**: 788, 1949.
64. Musser, J. H.: Primary Cancer of the Lung, Univ. of Pennsylvania Med. Bull. **16**: 289, 1903-04.
65. Acevedo, R. C., Giuntini, L. S., and Croxatto, O. C.: Consideration About a Case of Pulmonary Adenomatosis, An. Cáted. de pat. y clín. tuberc. **6**: 345, 1944.
66. Hatfield, W. H., and Hill, J. E.: Pulmonary Adenomatosis with a New Laboratory Finding, Am. J. Roentgenol. **62**: 525, 1949.
67. Smith, R. R., Knudtson, K. P., and Watson, W. L.: Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung, Cancer **2**: 972, 1949.
68. Gagné, F.: Primary Diffuse Alveolar Epithelioma of the Lungs, Pulmonary Pseudo-Adenomatosis; A Recent Observation, Bull. Assoc. franç. étude cancer **37**: 266, 1950.

69. Paul, L. W., and Juhl, J. H.: Pulmonary Adenomatosis, Further Roentgen Observations, Radiology **55:** 681, 1950.
70. Dunham, H. H., and Smith, V. G.: Terminal Bronchiolar or "Alveolar Cell" Carcinoma of Lung; A Case Report, J. Kansas M. Soc. **53:** 117, 1952.
71. Papanicolaou, G. N.: Personal communication to Watson and Smith.[58]
72. McDonald, J. R., and Woolner, L. B.: Cytologic Examination of Sputum and Bronchial Secretion in Diagnosis of Bronchogenic Carcinoma, Surg., Gynec. & Obst. **88:** 676, 1949.
73. Frissell, L. F., and Knox, L. C.: Primary Carcinoma of the Lung, Am. J. Cancer **30:** 219, 1937.
74. Tillett, R. S., and Hirsch, E. F.: So-Called Pulmonary Adenomatosis of the Lungs, Illinois M. J. **101:** 232, 1952.
75. Gepts, W.: Pulmonary Adenomatosis; Report of a Case Demonstrating Peculiar Histological Changes in Certain Bronchioles, Arch. Path. **52:** 473, 1951.
76. Schuster, N. H.: The Aetiology and Pathology of Primary Lung Tumors, J. Path. & Bact. **32:** 799, 1929.
77. Eismayer, G.: Concerning Primary Colloid Carcinoma of the Lung, Ztschr. f. Krebsforsch. **21:** 203, 1924.
78. Lindberg, K.: Formal Genesis of Pulmonary Cancer, Arb. a. d. path. Inst. d. Univ. Helsingfors **9:** 1, 1935. (Quoted by Neubuerger and Geever.[17])
79. Bass, H. E., and Singer, E.: Co-existing Lobar Adenocarcinoma and Cystic Disease of the Lung, Ann. Int. Med. **34:** 498, 1951.
80. Clagett, O. T.: Discussion of Stephens and Shipman.[22]
81. Osserman, K. E., and Neuhof, H.: Mucocellular Papillary Adenocarcinoma of Lung and Lobectomy, J. THORACIC SURG. **15:** 272, 1946; Mucocellular Papillary Adenocarcinoma of the Lung; Lobectomy, Five-Year Follow-Up, J. THORACIC SURG. **19:** 875, 1950.
82. Couch, R. S. C., Fleming, P. R., and Harrison, R. T. T.: A Case of Alveolar Cell Tumor of the Lung, Middlesex Hosp. J. **45-47:** 33, 1945-47.
83. Hildebrand, E.: Pulmonary Adenomatosis; Report of a Case, Am. Rev. Tuberc. **57:** 281, 1948.
84. McCallum, R. I.: Alveolar Cell Tumor of the Lung; Report of a Case, Brit. J. Tuberc. **42-43:** 90, 1948-49.
85. Effert, S.: Primary Diffuse Alveolar Epithelial Carcinoma; Case, Zentralbl. allg. Path. **85:** 162, 1949.
86. Liavaag, K.: So-Called Alveolar Cell Tumor, Nord. Med. **42:** 1276, 1949.
87. Moyer, J. H.: Pulmonary Alveolar Adenomatosis, Am. Rev. Tuberc. **61:** 131, 1950.
88. Rosemond, G. P., Boucot, K. R., and Aegerter, E.: Solitary Pulmonary Adenoma (Focal Pulmonary Adenomatosis); A Three-Year Follow-Up after Resection, J. THORACIC SURG. **22:** 99, 1951.
89. Voluter, G., and Rywlin, A.: Primary Unilateral Alveolar Cancer of the Lungs, J. radiol. électr. **32:** 826, 1951.
90. Fisher, J. H., and Holley, W. J.: Primary Alveolar Cell Carcinoma of the Lung, Arch. Path. **55:** 162, 1953.

DISCUSSION

DR. H. BRODIE STEPHENS, San Francisco.—I am certain that the Association is grateful to Captain Storey for this thoughtful study of a neoplasm that he terms alveolar carcinoma. Some of you will recall that Dr. Shipman and I reported a case and termed it pulmonary alveolar adenomatosis; this neoplasm occurred in a housewife 51 years of age who had been operated upon in 1948. We reported this case at the New Orleans meeting of the Association in 1949. This patient is still alive; she has demonstrated progressive pulmonary involvement, almost complete of the right lung by a snowy infiltrate, and of approximately the lower one-half of the left lung. Malignant cells have never been seen in the sputum from this patient; many sputum studies have been done.

(Slide.) I should like to review again the peculiar appearance of this particular tumor. This is a photograph of the right lower lobe; note the waxy appearance of the lung. It looks as if gelatin had been poured down into the bronchus and allowed to solidify. The disease was not in the regional lymph nodes and seemed to be confined to the right lower lobe at the time of operation.

(Slide.) This demonstrates the patchy involvement of the lung parenchyma. Normal alveoli are seen adjacent to the adenomatous area. The columnal cells forming the tumor appear to rest upon the alveolar framework yet do not invade across it.

(Slide.) Here is the high-power photomicrograph. These cells, you will notice if you study them carefully, do not completely encircle the alveolar framework. They are columnar cells, goblet in type, secreting mucus. They appear similar to those Dr. Storey has shown today.

Our own Dr. Graham laid down certain criteria for the diagnosis of alveolar-cell carcinoma, stating that the tumor reproduced the alveolar structure of the lung. There is no evidence that such has taken place in the tumor presented by Dr. Shipman and myself. Our patient had symptoms for at least seven years prior to operation; it is now five years since operation, so our patient has had a history of about twelve years' duration. She has never demonstrated any palpable lymph node involvement, and we still cannot find abnormal cells in the sputum. So perhaps there are variants of this so-called alveolar-cell carcinoma, or perhaps there are several distinct entities.

DR. FRANK S. ASHBURN, Washington, D. C.—I too have enjoyed Captain Storey's dissertation very much. We have had experience with three cases of this condition, and I want to show the slides on one of them.

(Slide.) This is the gross specimen showing the changes similar to those described by Captain Storey, and it is very surprising in our experience to come upon such a thing.

(Slide.) The percentage of mucus in these cells is larger than in the section shown by the previous speakers. However, you will notice here a very similar arrangement and configuration of the cells, the large tombstone cells containing large amounts of mucus.

Our experience certainly corroborates Captain Storey's findings relative to the frequency and accuracy of the diagnosis of the condition by cytologic examination of either sputum or bronchial secretions. I think it well to stress that in the hands of good men this is a very helpful diagnostic tool. I am not at all satisfied with the conclusions that local excision of such lesions constitutes adequate therapy. Of course, my experience is not large enough to draw a final conclusion as to what we can do with these lesions; since Captain Storey's figures seem to me to be based largely on material of which the greater part was obtained at autopsy, I would like to ask the extent of radical excision that has to be done and ask the men with wide experience to answer that question for us if possible.

DR. GABRIEL SELEY, New York.—I agree with Captain Storey's conclusion that alveolar-cell tumors, pulmonary adenomatosis, and carcinoma of the lung are different variants of the same disease. About one year ago Dr. Touroff and I had a 45-year-old patient who presented herself because of a single nodule in the right upper lobe. There were no pulmonary symptoms. Chest roentgenograms taken two years before admission were negative. Nine months before admission during a routine examination a small nodule measuring about 3 by 2 cm. was noted in the anterior segment of the right upper lobe very similar to the one Captain Storey mentioned. Subsequent x-ray films showed a slight enlargement of this nodule and questionable cavitation. Sputum examinations were repeatedly negative for tubercle bacilli and tomograms failed to reveal any calcification.

At operation the nodule was excised by wedge resection for biopsy purposes. A frozen section was immediately reported as showing a pulmonary adenoma and a right upper lobe lobectomy was promptly performed. No nodes were noted at the hilus. The patient made an uneventful recovery and follow-up x-rays are negative for other foci. Further study of the specimen corroborated the frozen section report, and the final diagnosis was pulmonary adenoma of alveolar-cell type without evidence of malignancy. I am simply giving the pathologist's statement.

This case, then, represents a single, early, possibly benign focus of disease which, if left in, may go on to malignant changes and dissemination throughout both lungs. It is further evidence against a multicentric origin for these tumors, and I certainly feel that the minimal resection in these cases should be a lobectomy.

DR. WILLIAM L. WATSON, New York.—We saw our first patient with so-called alveolar-cell carcinoma in 1932. Since then we have been seeing them with increasing frequency. I have one patient about whom I would like to tell you because it may add some information regarding the life history of this unusual tumor.

(Slide.) This is the film of a 65-year-old nurse in our hospital who consulted the medical service because of a cough and a slight fever in December, 1949. She received symptomatic treatment, and a routine x-ray examination of the chest was taken which showed a small area of increased density in the right lower lung field. The symptoms cleared up and she was allowed to go back to work in the operating room.

(Slide.) About two months later another roentgenogram of the chest was taken and it again revealed a mass in the right lower lung field.

(Slide.) Four months later another film was taken and showed an enlargement of the mass density.

(Slide.) Six months later another film was taken and in 1951 still another film was taken. In March, 1952, two years and four months after the original x-ray film, the patient was referred to the thoracic surgical service. Bronchoscopy was done and it was entirely negative except that we washed the bronchus out and Dr. Papanicolaou studied these washings and said it was loaded with cancer cells, probably of the alveolar-cell type. A pneumonectomy was done.

(Slide.) The bronchi from the major bronchus on down were opened and no primary tumor of bronchial origin could be elicited. The tumor, as you see, is out in the periphery, and it is a typical so-called "terminal bronchiolar or alveolar-cell carcinoma." We did a complete pneumonectomy and node dissection, and the nodes were negative.

(Slide.) We have 60 of these patients with alveolar-cell cancer and have done 34 operations; 18 pneumonectomies, 4 lobectomies, 2 segmental resections, and 10 exploratory thoracotomies. The operability rate is 57 per cent, but the resectability rate is 70 per cent.

(Slide.) Of the 18 patients having pneumonectomy, 8 are alive, 1 for five years, 2 for two years, and 5 for one year or less. With lobectomy, the number of patients alive, 4; number of patients operated on, 4; 1 alive for eight years, 2 for two years, and 1 for one year.

(Slide.) This salvage rate in the group operated upon more than five years ago shows the inaccuracy of all statistics. Here we have a 40 per cent five-year cure rate of this tumor by excisional surgery. None were cured by x-ray therapy, and none survived who had no treatment at all. In addition we have found that 21 per cent of our 60 patients did not have any symptoms prior to the time the cancer was picked up on routine chest examination.

CAPTAIN STOREY (Closing).—I wish to thank all the discussers for their interesting comments. Our experience with cytologic studies of the sputum in patients with bronchiolar carcinoma has been somewhat similar to that of Dr. Stephens. We have not had quite as good results with the Papanicolaou examination in our personal cases as Dr. Watson and his group have had at Memorial Hospital, nor have we been as successful in making a diagnosis by this means as Dr. MacDonald and his associates at the Mayo Clinic. I have personally studied many histologic sections from a large number of these lesions and I know that the picture varies considerably.

It is my opinion that whether the Papanicolaou is positive or negative is probably influenced considerably by the extent of the papillary projections within the alveoli. These are the tiny fragments of tumor which break off, are expectorated, and can be recognized histologically, not only as tumor cells, but in some cases it is possible for the pathologist to suggest the specific diagnosis of bronchiolar carcinoma when they are seen in the Papanicolaou preparation. The individual cells themselves are frequently quite benign in appearance and I believe that unless clumps of cells, as MacDonald and Woolner have described, are found, the most competent pathologist would be quite reluctant to

make the diagnosis of pulmonary malignancy in this group of patients. The isolated cells are usually of uniform size and shape, their nuclei are normal and the nuclear-cytoplasmic ratio is also commonly normal.

I am pleased to hear Dr. Ashburn's comments. I do not pretend to have had sufficient experience to provide a categorical answer to the question as to the extent of excisional surgery which is indicated in the treatment of this disease. However, I have been able to find in the literature reports of 218 cases of bronchiolar carcinoma, including those which we are reporting, and have personally reviewed each of the original case reports. A statistical analysis of those cases will appear in the published manuscript. Of particular interest are the figures relative to metastases in these lesions. Among the reported cases, metastases occurred in roughly 50 per cent of the cases; 54 per cent is the precise figure, I believe. Among those patients who have metastases, mediastinal involvement alone was present in only one-third; one-third showed both local and distant metastases, and the remaining one-third showed distant spread only. These figures make it seem rather illogical to me to perform surgery of a radical nature unless the local conditions found at operation so dictate. Obviously, if one finds mediastinal nodes, proved to be malignant on frozen section examination, or even enlarged firm nodes which would arouse a suspicion of carcinoma by their gross appearance, more radical operation would be indicated.

In spite of what is said in the published abstract of my paper, and even though I do have one patient whom I treated by segmental resection who is alive and without evidence of disease nineteen months following operation, I have come to agree with Dr. Seley's comment that a lobectomy should probably be the minimum operation in patients with this disease. I personally do not intend to treat any future patients who have this tumor by segmental resection. In reviewing many histologic sections from these lesions I have seen tumor cells in the pulmonary lymphatics, both subpleural and perivascular, too frequently to make me feel comfortable in undertaking a really small localized operation for this neoplasm.

THE SIGNIFICANCE OF PULMONARY HYPERTENSION AS A CAUSE OF DEATH FOLLOWING PULMONARY RESECTION

WILLIAM E. ADAMS, M.D., JOHN F. PERKINS, JR., M.D. (BY INVITATION), ADOLFO FLORES, M.D. (BY INVITATION), PAUL CHAO, M.D. (BY INVITATION), AND MIGUEL CASTELLANOS, M.D. (BY INVITATION)
CHICAGO, ILL.

IN MAN, under normal conditions, the pulmonary reserve is several times that necessary to meet the requirements of the body while at rest. Evidence of this is demonstrated by the ability of patients to tolerate removal of one lung. Moreover, it is possible to withstand the resection of more than one-half of both lungs when this is performed in stages. In dogs, the reduction of lung capacity to as little as one upper lobe (approximately 15 per cent of the total lung volume) may be successfully accomplished by bronchial stenosis, when produced in stages over a period of several months.[1]

In patients with bilateral alteration of the lung due to inflammatory, degenerative, or other conditions, the pulmonary capacity may be considerably reduced. This is especially true in the so-called older age group. In nonmalignant disease it is possible to limit pulmonary resection, thus preserving maximum lung function. However, in the case of malignant lesions, it has been generally believed that removal of the entire lung along with adjacent tumor-bearing tissue is the operation of choice when it can be tolerated by the patient.[2] Since the risk of pneumonectomy is increased in the older age group having poor pulmonary reserve, repeated attempts have been made to determine the "resection tolerance" of such patients prior to operation. Studies made by a number of investigators have increased our knowledge of factors concerned with this problem. Recently, special attention has been given to the problem of changes in pulmonary tension attending the resection of lung tissue both in animals and in man.[3-6] Cardiac catheterization, although practiced for some time, has been made much more practical in recent years and has contributed much to these investigations. Most of the publications dealing with this problem have been concerned with patients in whom pulmonary resection was made for various conditions. There has therefore been little opportunity to study the alterations in cardiopulmonary function attending lung resection where maximal "resection tolerance" has been reached.

The present report deals chiefly with experiments in which pulmonary resection was carried out to the limit of tolerance without loss of the animal. The experiments were designed to determine the role played by the vascular element (perfusion) versus the pulmonary element (diffusion) of the lung as a significant factor in the cause of death after pulmonary resection and also to investigate the various factors which influence pulmonary tension.

From the Departments of Surgery and Physiology of the University of Chicago.

This work was supported in part by United States Public Health Grant No. RG1254(C) and in part by the Douglas Smith Foundation for Medical Research of the University of Chicago.

Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

In earlier communications[7, 8] it was shown that a rise in pulmonary artery tension could be expected in dogs after the removal of one lung. The average elevation in tension in a group of thirty dogs was from an original of 32/5 to 44/5 mm. Hg following operation. This increase in pulmonary tension was maintained for at least several months. In a second group of thirteen dogs where pulmonary resection was extended in stages to include the entire lung with the exception of one upper lobe, the pulmonary tension increased from an original average of 40/5 to an average of 64/8 mm. Hg following surgery. Thus the pulmonary artery pressure was doubled (32/5 to 64/8). Some of these animals died of spontaneous pneumothorax or of infection; however, most of them at autopsy demonstrated evidence of cardiac failure, a bloody, frothy material in the tracheobronchial tree and edema of the lungs being found. Four of the animals survived this extensive pulmonary resection.

An attempt was made to increase the survival rate by the use of a plastic sponge prosthesis in the pleural space following the initial operation which was a total pneumonectomy. This procedure failed completely since the elevation in pulmonary artery pressure was even greater in these animals following the second operation. None of this group of ten dogs survived.

EXPERIMENTAL METHODS

Ten healthy mongrel dogs weighing from 10 to 15 kilograms were used. A total right or left pneumonectomy had been made six to twelve months prior to the studies now being reported. Anesthesia for the final operation consisted of intravenous pentobarbital sodium 30 to 35 mg. per kilogram with intratracheal positive pressure oxygen, or ether-oxygen without the barbiturate. Prior to operation on the chest a No. 8F cardiac catheter was introduced under fluoroscopic control into a pulmonary artery via an external jugular vein. Heparin (0.5 mg. per cubic centimeter of saline) was used to maintain a patent catheter. In earlier experiments, pressures were measured with a Hamilton manometer or with a Sanborn electromanometer. In the present study, mean pressures only were measured by means of a saline manometer. Anesthetic agents and oxygen mixtures were administered through an intratracheal catheter under positive pressure or through a tracheotomy tube.

Continuous recording of arterial blood oxygen saturation was made by means of an oximeter cuvette inserted between a carotid artery and an external jugular vein and connected to a recording oximeter designed by one of us (J. F. P.) and constructed in the physiology laboratory.[9] Heparin, 5.0 mg. per kilogram, intravenously, and 5.0 mg. per kilogram, intramuscularly, was used to prevent clotting when the cuvette was connected.

The chest was opened through the fifth interspace and an occlusion unit was placed around the pulmonary artery immediately below the branches to the left or right upper lobe. Thus, occlusion of the vessel at this point would reduce the total pulmonary function to one upper lobe or approximately 15 per cent of normal. In some animals a second occlusion unit was placed around the bronchus at the same level. The occlusion units consisted of a loop of heavy braided silk passed around the artery or bronchus, then introduced into a

polyethylene tube, and both brought out through a small puncture wound in the chest wall. These tubes were filled with petroleum jelly and also clamped to avoid a pneumothorax. A small rubber catheter for maintaining expansion of the lung was also brought out through a puncture wound.

In order to demonstrate more striking changes in pulmonary tension or arterial oxygen saturation when the pulmonary capacity was suddenly reduced to a maximum tolerance level, an apparatus for exercising the animal was constructed and connected to all four extremities. Exercise consisted of intermittent (60 per minute) electrically stimulated contractions of the shoulder girdle and the thigh muscles. A moderate to vigorous degree of exercise was used.

Employing this described arrangement, changes in pulmonary artery tension and arterial blood oxygen saturation were determined under the following conditions:

A. Dog at rest breathing air.

B. Dog at rest breathing air with lung capacity reduced to 15 per cent.

C. Dog at rest breathing oxygen (100 per cent).

D. Dog at rest breathing oxygen (100 per cent) with lung capacity reduced to 15 per cent.

E. Dog exercising while breathing air.

F. Dog exercising while breathing air with lung capacity reduced to 15 per cent.

G. Dog exercising while breathing oxygen (100 per cent).

H. Dog exercising while breathing oxygen (100 per cent) with lung capacity reduced to 15 per cent.

RESULTS

A. With the Animal at Rest and Breathing Air.—Both pulmonary artery pressure and blood oxygen saturation varied considerably with the depth of anesthesia and with the degree of activity of the animal. Oxygen saturation varied from 66 to 90 per cent. The usual saturation was 89.5 per cent. Pulmonary artery pressure varied from 20.5 to 43.0 cm. saline.

C. With the Animal at Rest and Breathing 100 Per Cent Oxygen.—The pulmonary artery tension was the same as in *A* while breathing air. However, the blood oxygen saturation was elevated to as high as 100 per cent in some animals. The usual level for the group was 97.8 per cent.

B and D. With the Animal at Rest Breathing Air or Oxygen and With Lung Capacity Reduced to 15 Per Cent of Normal.—The effect on pulmonary artery tension was similar during both conditions. Under deep narcosis (with pentobarbital sodium) the increase in tension was as low as 4.5 cm. saline. The highest elevation was 35.5 cm. saline or 118.0 per cent of the original value. The usual elevation for the group was 31.2 cm. or 90.7 per cent.

Blood oxygen saturation was reduced very little when compared with the marked change in pulmonary tension. While breathing air the saturation fell from 3 to 6 per cent, or an average of 4.5 per cent when lung capacity was lowered to one lobe. While breathing oxygen no reduction in saturation was observed in some animals. The average fall for the group was 3.8 per cent.

E and F. Influence of Exercise Before and After Reducing Lung Capacity to 15 Per Cent While Breathing Air.—The effect of work on pulmonary artery tension in most animals was dramatic whether breathing air or 100 per cent oxygen. There was a rapid increase in tension averaging 14.7 cm. saline or 60 per cent, with one-half of the lung functioning, and 20 cm. saline or 80 per cent increase in tension after reduction to only one lobe. Thus when the effect of exercise was added to the effect of reduction of capacity from one lung down to one lobe, the pulmonary tension was elevated over 200 per cent in some animals.

Blood oxygen saturation remained unchanged in two dogs, while in the remainder there was as much as an 18 per cent fall, with an average of 8 per cent decrease, before reduction of lung capacity. The oxygen saturation fell as much as 19 to 50 per cent, with an average of 29.6 per cent, when only one lobe was functioning.

When breathing 100 per cent oxygen, blood saturation was little affected by exercise, irrespective of whether lung capacity was 50 or 15 per cent of normal. Pulmonary artery pressures, however, were altered by exercise in amounts similar to those occurring when the animals were breathing air.

DISCUSSION

Figs. 1 and 2 (Dog 36) show systolic and diastolic right ventricular pressure curves during a right pneumonectomy and subsequently during a left lower lobectomy. The systolic pressure during right pneumonectomy became elevated by approximately 30 per cent. This elevation persisted during the several months intervening between the two stages. At the end of the second stage the systolic pressure was elevated approximately 75 per cent over that at the beginning of this procedure. However, this (80 mm. Hg) was more than 150 per cent above the level at the beginning of the first operation (30 mm. Hg). The curves shown on this dog were quite characteristic of the group reported in a former communication.[7]

As noted previously, while at rest and breathing air the pulmonary tension in most animals became elevated by as much as 90 per cent when lung capacity was reduced. In some animals it was increased over 100 per cent. At the same time the saturation in arterial blood oxygen was decreased by a relatively small amount, an average of 4.5 per cent. When 100 per cent oxygen was added to the inhaled mixture this decrease in saturation was minimal, or the level remained the same as that prior to reduction of lung capacity to 15 per cent. Fig. 3 (Dog 737) illustrates these points. Oxygen saturation was decreased approximately 5 per cent (88 to 83) when the lung capacity was reduced to one lobe. The right ventricular pressure, however, rose from 53 to 82 cm. of saline, representing an elevation of over 50 per cent.

Fig. 4 (Dog 737) illustrates the effect of oxygen and of exercise. While breathing 100 per cent oxygen there was no change in the level of blood oxygen saturation when the lung capacity was reduced. Likewise, when exercise was begun the saturation continued at a level of 100 per cent. On changing from

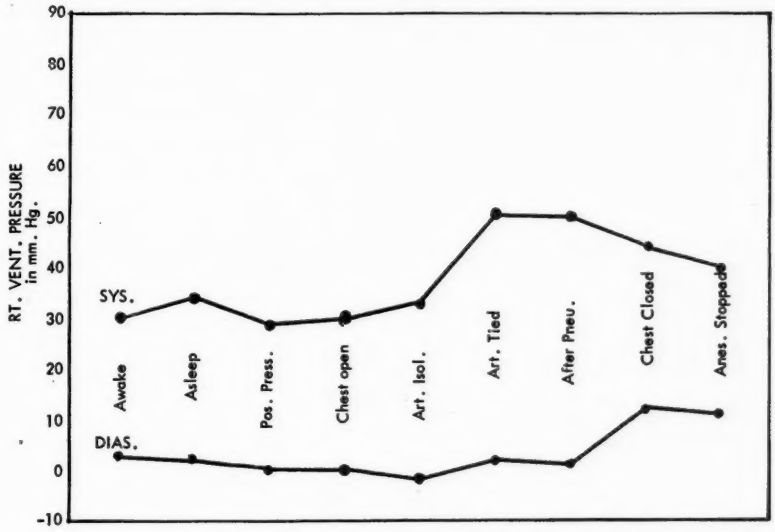


Fig. 1.—Dog 36. Shows systolic and diastolic right ventricular pressures during a right pneumonectomy. Note that the systolic pressure was elevated by approximately 30 per cent following the operation.

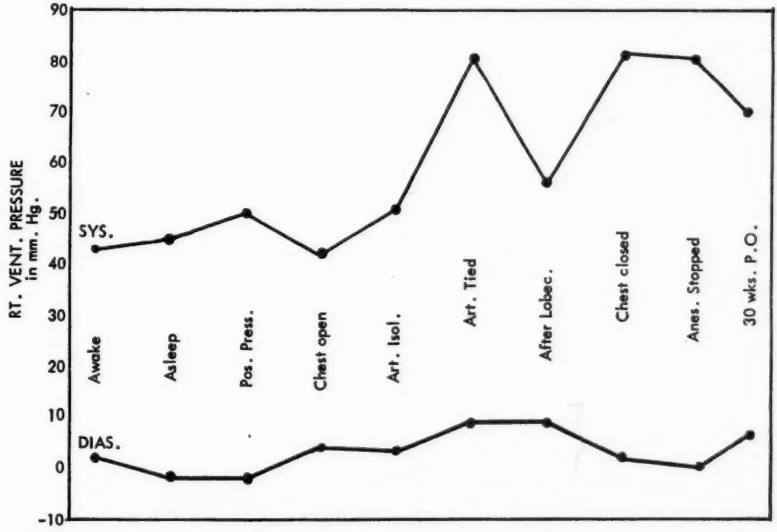


Fig. 2.—Dog 36. Shows systolic and diastolic right ventricular pressures during resection of the left lower lung lobe in a dog whose right lung had been resected six months previously. Note elevation of systolic pressure to a level of 80 mm. Hg which was 150 per cent above the level of pressure at the beginning of the first operation (30 mm. Hg).

100 per cent oxygen to air the saturation immediately fell dramatically to a level of 63 per cent and continued on downward in three minutes to 45 per cent. Release of the occlusion units restoring the lung capacity to 50 per cent produced a rise in oxygen saturation from 45 to 63 per cent. The right ventricular pressure in this animal had risen from an original level of 35 cm. saline to 96 cm. of saline after reduction of lung capacity combined with exercise. This represented an elevation of two and three-fourths times the original level, or 275 per cent.

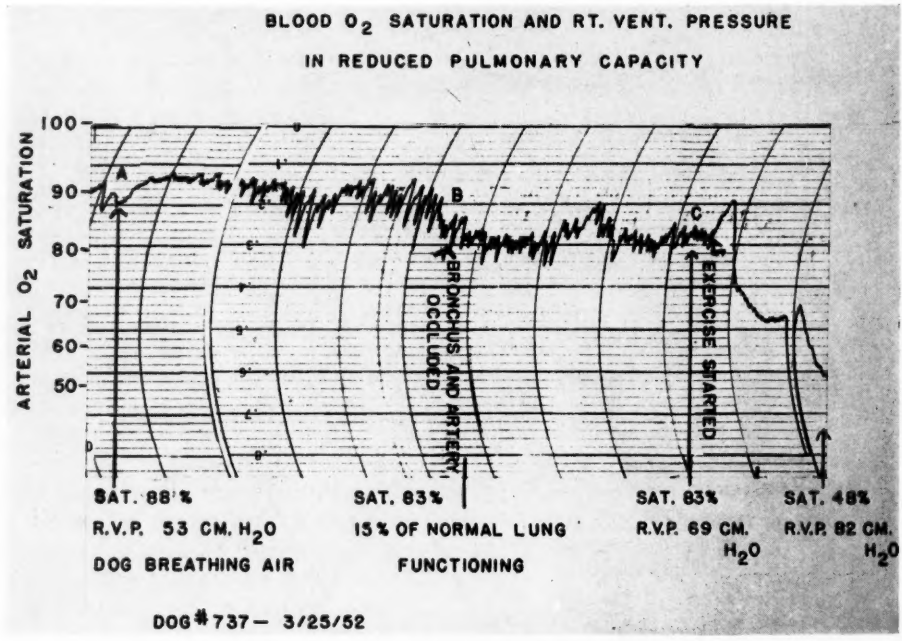


Fig. 3.—Dog 737. Shows a marked elevation in right ventricular pressure with reduction in lung capacity and exercise of the animal. Oxygen saturation was reduced by only 5 per cent when lung capacity was reduced to one upper lobe. The effect of exercise on oxygen saturation is demonstrated.

Fig. 5 (Dog 469) illustrates a fairly characteristic curve of blood oxygen saturation and pulmonary artery pressure during the various conditions studied in the experiment. There was a marked increase in pulmonary artery pressures on reduction of lung function in most instances with relatively little reduction in blood oxygen saturation until exercise was begun. Thereafter a greater amount of oxygen was required by the animal.

Fig. 6 (Dog 28) illustrates the effect of reduced lung capacity while receiving 100 per cent oxygen before and during exercise, and later while breathing air. There was no change in blood oxygen saturation as a result of either reduction of lung capacity or exercise while breathing oxygen. Pulmonary artery tension, however, increased from 48.5 to 68.5, an increase of almost 41

per cent. The blood oxygen saturation was lowered 7 per cent by reduction in lung capacity and 10 per cent by exercise, when the dog was breathing air.

Fig. 7 (Dog 469) illustrates the effect of exercise, inhalation of oxygen, and reduction of lung capacity on arterial blood oxygen saturation and right ventricular pressures. Exercise produced relatively little effect on blood oxygen saturation while the animal was breathing air before lung capacity had been reduced. Following reduction of lung capacity there was an immediate fall in saturation, from 85 to 55 per cent. On breathing 100 per cent oxygen the saturation immediately rose to 97 per cent within a period of less than a minute. During this time the right ventricular pressure became elevated from 20 to 50 cm. of water, an increase of 150 per cent.

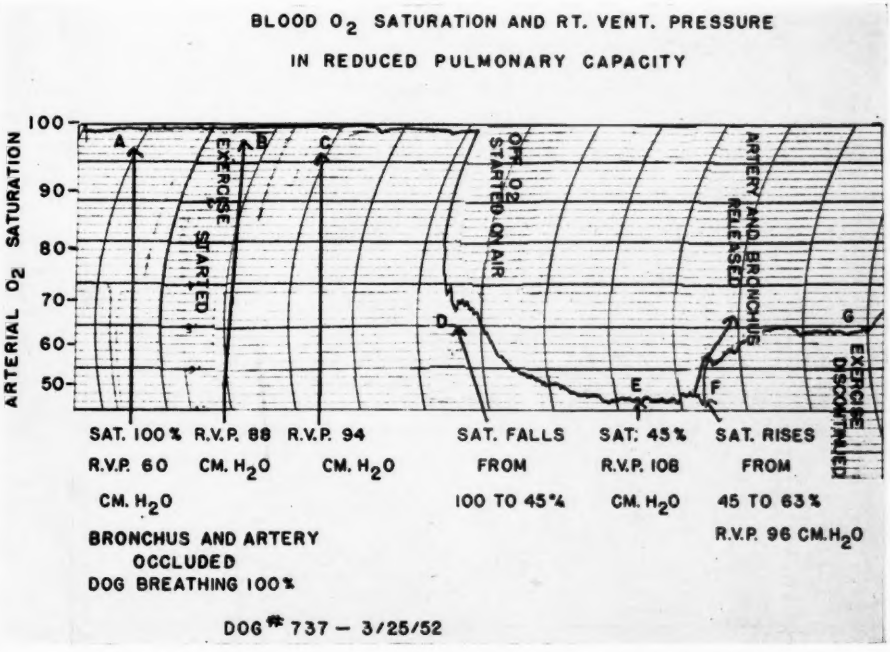


Fig. 4.—Dog. 737. Shows a complete lack of effect on blood oxygen saturation by either reduction of lung capacity to one lobe or on exercising the animal. The right ventricular pressure on the other hand became elevated 50 per cent. On breathing air there was a precipitant fall in oxygen saturation which did not return to the previous level when the capacity was returned from 15 to 50 per cent of normal.

The results of these experiments in conjunction with those reported in previous communications lend strong support to the belief that elevated pulmonary tension may be a significant factor in the cause of death following lung resection in patients with markedly reduced pulmonary reserve. The amount of reduction in lung capacity necessary to produce in dogs a serious level of pulmonary hypertension was found to be 80 to 85 per cent. In most animals this has been accompanied by an increase of 75 to 100 per cent in pulmonary artery pressure. Despite this fact, the accompanying decrease in blood oxygen

saturation has been relatively small, an average of only 4.5 per cent. These results support the view that the lung in a reduced reserve state, but without the presence of a physiologic arteriovenous shunt, may be able to adequately oxygenate the blood, but that the accompanying pulmonary hypertension may reach a critical level. In patients with some degree of pulmonary hypertension due to bilateral disease, a much greater pulmonary tension may follow the resection of one lung. Furthermore, such factors as anoxia and emotional strain may in themselves contribute to elevation in pulmonary tension as shown by Motley and his associates,[10] Duke and Killick,[12] and Cargill and Hickam.[11]

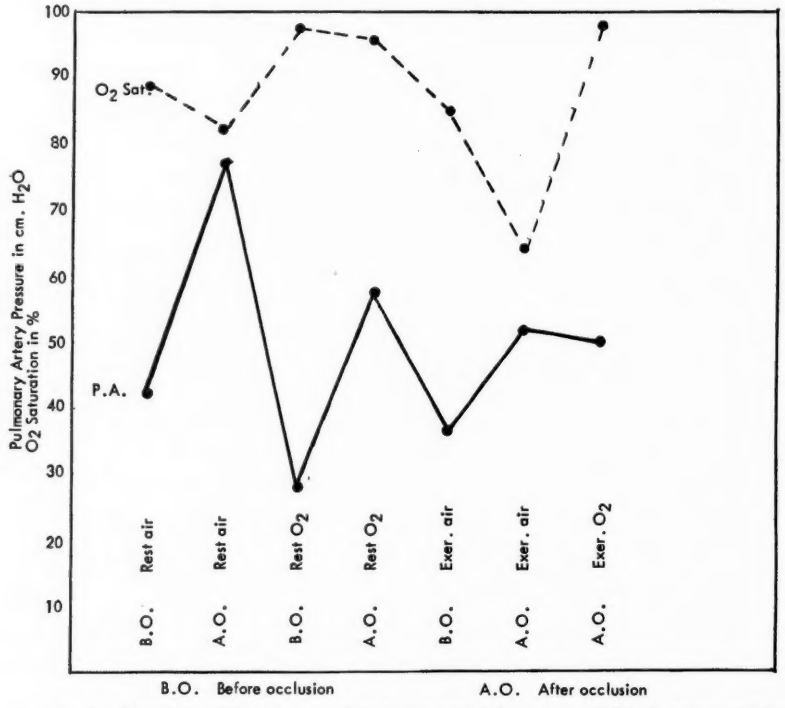


Fig. 5.—Dog 469. Illustrates a fairly characteristic curve of blood oxygen saturation and pulmonary artery pressure during the various conditions studied in the experiment. Note a marked increase in pulmonary artery pressure on reduction of lung capacity to 15 per cent (*I* upper lung lobe) with relatively little fall in oxygen saturation.

In animal experiments deep narcosis with pentobarbital sodium markedly lowered both blood oxygen saturation and pulmonary tension, whereas light ether anesthesia and muscular activity of the animal during induction produced an elevation in pulmonary tension.

Since anoxia may play a major role in the elevation of pulmonary tension, it may be an additional factor of importance both during anesthetic induction accompanied by respiratory depression or spasm as well as during the course of operation if oxygenation is not constantly maintained at an adequate level.

It is also well known that either collapse of the lung or overdistension of the lung impedes the flow of blood through the lesser circulation, thus tending toward increase in pulmonary tension. In patients with low pulmonary reserve it is imperative that optimum inflation of the lung be maintained while the chest is open. Following operation, retention of bronchial secretions, accompanied by atelectasis and pneumonitis, or by a physiologic shunt, increases the hazards from anoxia and pulmonary hypertension.

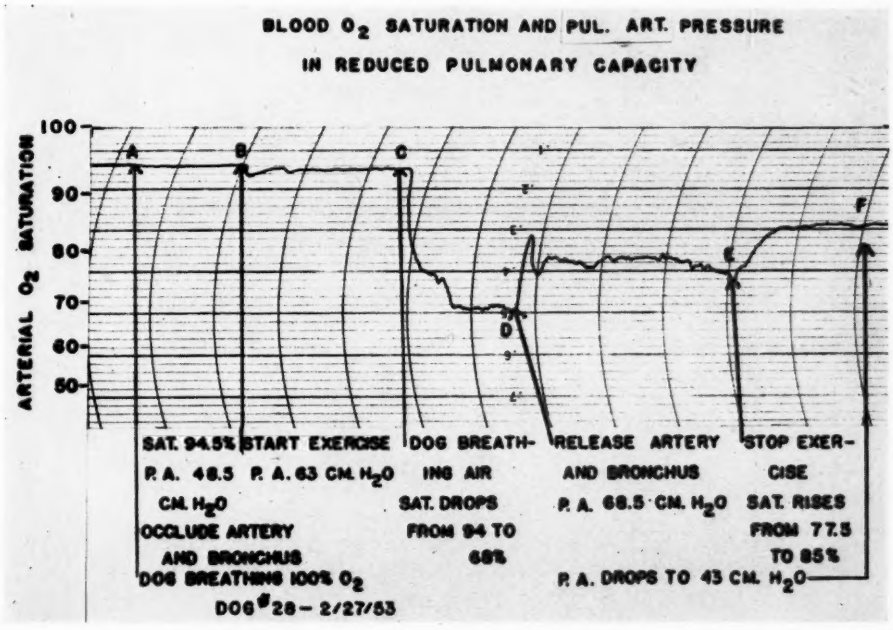


Fig. 6.—Dog 28. Note the lack of change in blood oxygen saturation as a result of reduction in capacity or as a result of exercise while breathing oxygen. The pulmonary artery tension however increased from 48 to 68 cm. of saline. On breathing air the saturation dropped markedly and did not recover on increase of lung capacity and cessation of exercise.

Resection of a lung containing anatomic or physiologic arteriovenous fistulas (shunts) may also cause an elevation of pulmonary tension as illustrated by a patient in Fig. 8. The tension was increased with closure of each arteriovenous shunt. In spite of the fact that this patient previously had a pneumonectomy on the opposite side for the same lesion, his original pressure in the right ventricle after induction of anesthesia was complete, was only 25/10 mm. of mercury. At the conclusion of the operation the pressures were 45/0 mm. of mercury. Thus, with the closure of three arteriovenous fistulas the systolic pressure was elevated 80 per cent.

Our findings (Table I) and those of others[5] would indicate that severe pulmonary hypertension occurs infrequently. However, most studies on human beings have been made with the patient at rest and have not included a number

TABLE I. PULMONARY ARTERY PRESSURES* BEFORE AND FOLLOWING OCCLUSION OF THIS VESSEL IN PULMONARY RESECTION

PATIENT	AGE	SEX	DIAGNOSIS AND OPERATION	PRESSURE IN CM. SALINE	
				BEFORE OCC.	AFTER OCC.
1. E. W.	23	M	Bronchial adenoma—pneumonectomy	38.5	38.5
2. P. G.	74	M	Carcinoma and tuberculosis—pneumonectomy	35.0	43.0
3. L. R.	54	M	Carcinoma—pneumonectomy	21.6	21.6
4. G. D.	53	M	Cavitary silicosis—pneumonectomy	42.0	53.0
5. T. C.	67	M	Carcinoma—lobectomy	34.0	37.0
6. J. V.	45	M	Lung abscess—pneumonectomy	22.5	28.5
7. L. G.	41	F	Bronchiectasis—bilateral resection		40/21.5-70/50‡
8. R. R.†	31	M	Multiple A-V fistula—pneumonectomy, 1943 (small resections of right upper, middle, and lower lobes)	27.5/10 B.P.: 100/60	45/0‡ 90/60

*Pressures recorded except in 7 and 8.
†Catheter became dislodged into right ventricle.
‡Pressures in mm. Hg.

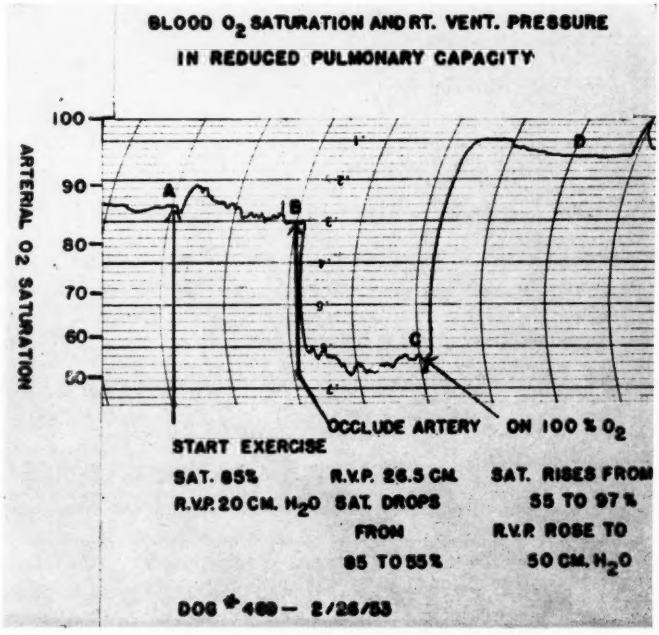


Fig. 7.—Dog 469. Exercise altered the blood oxygen saturation but little while the animal was breathing air. Exercise plus reduction of capacity produced a sudden drop in saturation which immediately recovered on changing from inhalation of air to 100 per cent oxygen. The right ventricular pressure increased from 20 to 50 cm. of saline or 150 per cent, with reduction of capacity and exercise.

of factors during the early postoperative course which may influence considerably the level of pulmonary tension. When pulmonary hypertension does develop it may very well be the most significant factor in the outcome of some patients following pulmonary resection. Measurement of pulmonary tension at operation may provide information for guidance of the management both during and following surgery.

SUMMARY AND CONCLUSIONS

1. Pulmonary hypertension of serious import may be produced in dogs by resection of 80 to 85 per cent of the lung.

2. The accompanying fall in blood oxygen saturation is small (average 4.5 per cent) in view of the severity of the pulmonary hypertension.

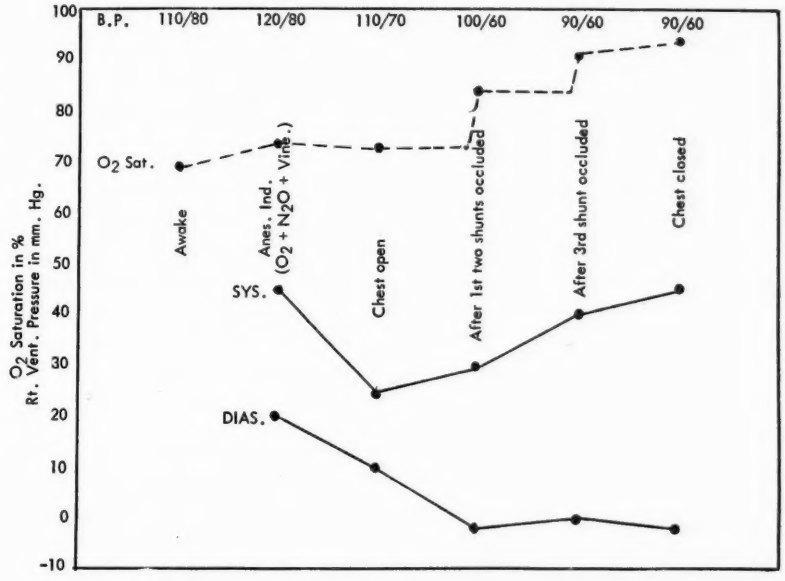


Fig. 8.—R. R. No. 301288. Closure of A-V fistulas of the lung. Correlation or right ventricular pressures with arterial blood oxygen saturation and systemic arterial pressures in a patient during the closure of three arteriovenous fistulas of the right lung. The left lung had previously been removed for the same type of lesion.

3. When a demand for more oxygen was produced through exercise, a more severe grade of pulmonary hypertension as well as a much greater reduction in blood oxygen saturation developed.

4. Inhalation of 100 per cent oxygen restored to a normal level the lowered blood oxygen saturation produced by exercise and reduced lung capacity but did not alter the severity of the degree of pulmonary hypertension.

5. Determination of pulmonary tension at operation may aid in both operative and postoperative management.

We wish to thank Mr. Willard Webber for technical assistance.

REFERENCES

1. Adams, W. E.: Subtotal Atelectasis and Pneumonectomy in Dogs, Proc. Soc. Exper. Biol. & Med. **28**: 957-958, 1931.
2. Churchill, Edward D., Sweet, Richard H., Soutter, Lamar, and Scannell, J. Gordon: The Surgical Management of Carcinoma of the Lung. A Study of the Cases Treated at the Massachusetts General Hospital from 1930 to 1950, J. THORACIC SURG. **20**: 349-365, 1950.
3. Cournand, A., Riley, R. L., Himmelstein, A., Austrian, R.: Pulmonary Circulation and Alveolar Ventilation—Perfusion Relationships After Pneumonectomy, J. THORACIC SURG. **19**: 80-116, 1950.

4. Scarff, J. E.: Pulmonary Blood Pressures, Arch. Surg. **12**: 591, 1926.
5. Mendelsohn, Harvey J., and Zimmerman, Henry A.: A Study of Pulmonary Hemodynamics During Pulmonary Resection, J. THORACIC SURG. **20**: 366, 1950.
6. Riley, R. L., Himmelstein, A., Motley, H. L., Weiner, H. M., and Cournand, A.: Studies of Pulmonary Circulation at Rest and During Exercise in Normal Individuals and in Patients With Chronic Pulmonary Disease, Am. J. Physiol. **152**: 372, 1948.
7. Carlson, Ralph F., Charbon, Bernard C., Charbon, Harmia G. A., and Adams, W. E.: The Effect of Decreasing the Amount of Lung Tissue on the Right Ventricular Pressures in Animals, J. THORACIC SURG. **21**: 621, 1951.
8. Charbon, Bernard C., and Adams, William E.: A Study to Determine the Effect of Prevention of Overdistention of the Remaining Lung Tissue on the Elevated Right Ventricular Pressures Following the Resection of Lung Tissue in Dogs, J. THORACIC SURG. **23**: 341, 1952.
9. Perkins, John F., Jr., Adams, William E., and Livingstone, Huberta: The Conversion of Millikan and Wood Type Oximeters Into Direct-Writing Recording Instruments for Use in Surgery, in Studies of Pulmonary Function, and in Teaching Respiratory Physiology, J. Lab. & Clin. Med. **40**: 457-478, 1952.
10. Motley, H. L., Cournand, A., Werkö, L., Himmelstein, A., and Dresdale, D.: Influence of Short Periods of Induced Acute Anoxia Upon Pulmonary Artery Pressure in Man, Am. J. Physiol. **150**: 315, 1947.
11. Hickam, J. B., and Cargill, W. H.: Effects of Exercise on Cardiac Output and Pulmonary Arterial Pressure in Normal Persons and Patients With Cardiovascular Disease and Pulmonary Emphysema, J. Clin. Investigation **27**: 10, 1948.
12. Duke, Helen N., and Killick, Esther M.: Pulmonary Vasomotor Responses of Isolated Perfused Cat Lungs to Anoxia, J. Physiol. **117**: 303, 1952.

DISCUSSION

DR. AARON HIMMELSTEIN, New York.—We have been interested in the problems of pulmonary hypertension in Dr. Cournand's laboratory for some time. I think that in speaking of pulmonary hypertension we should remember two things—that is, that pressure varies with flow and varies with resistance. In Dr. Adams' experiments he is trying, I believe, to define the maximum of pulmonary tissue that one can leave after resection and produce hypertension at rest.

We have measured the flow in patients who had a pneumonectomy. At rest, when the flow is presumably minimal no hypertension was found. When these patients are exercised it was regularly demonstrated that hypertension developed as flow increased. The ability of a normal pulmonary vascular bed to absorb an increase in flow without a rise in pressure apparently extends to about a threefold increase in flow, which in the normal is never reached. However, when a patient has a pneumonectomy all the flow is immediately doubled through the remaining pulmonary artery, and mild exercise raises the flow above a threefold increase and causes hypertension.

We have been interested too in whether bilateral resections of the amount of pulmonary tissue that is comparable to a pneumonectomy, in which the pulmonary vascular bed in distended lung occupying both chests has the same effect as does pneumonectomy. In Captain Storey's department at St. Albans Naval Hospital I am familiar with the pursuit of this information, and the results are essentially similar to those found in the group of pneumonectomies that we studied.

DR. ADAMS (Closing).—It is, of course, realized that in animals we are able to control the nature of the lung better than is possible in a human being, and in problems dealing with inflammatory or degenerative disease we have a combination of factors playing a role. As Dr. Himmelstein has pointed out, we have cut down the lesser circulation until elevation in pressure resulted. However, it seems to me that unless we have a physiologic shunt operating, and we frequently do in human beings, the effect of reduced pulmonary capacity on blood oxygen saturation is not going to be as detrimental as is the effect on pulmonary artery pressure. As was indicated this morning, we are constantly faced with problems dealing with markedly lowered pulmonary reserve. If we can get information that will give us the true status of both the vascular and the pulmonary factors, we can then do a much better job for our patients.

PREVENTION OF CHEST WALL DEFECTS: USE OF TANTALUM AND STEEL MESH

DONALD B. EFFLER, M.D.
CLEVELAND, OHIO

SURGICAL removal of a malignant chest wall tumor is best accomplished by radical block excision allowing a wide margin of normal tissue on all sides of the resected specimen. Failure to provide an adequate tissue margin will enhance the prospect of local recurrence and decrease the possibility of cure.

The principle of block excision has been applied to the chest wall for years;[1-3] successful removal of large segments of the bony thorax and related soft parts is no longer a momentous undertaking when adequate supportive measures are available.

Defects of the chest wall following surgery or trauma may pose a serious problem. To cure the patient of malignant disease, it has been necessary to disregard the resultant chest wall deformity; nevertheless, the creation of an extensive defect has been a deterrent and too often has resulted in a compromise operation.

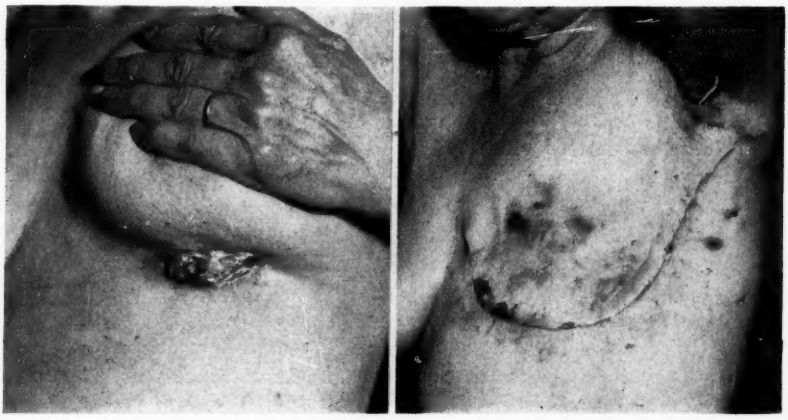
Frequently, the surgeon has observed that the patient tolerated the definitive operation much better than the resultant postoperative defect.

In addition to an unsightly deformity, there may be serious disturbances of respiratory physiology. An unsupported chest wall is associated with parodoxical respiration which may incapacitate the patient who has low pulmonary reserve. Improper ventilation of the affected pulmonary tissue is manifested by an increase in the pulse and the respiratory rate, particularly in the older patient. This has been attributed to a localized accumulation of alveolar carbon dioxide in that portion of the lung hampered by parodoxical respiration. The cough reflex is also impaired, further compromising the respiratory system.

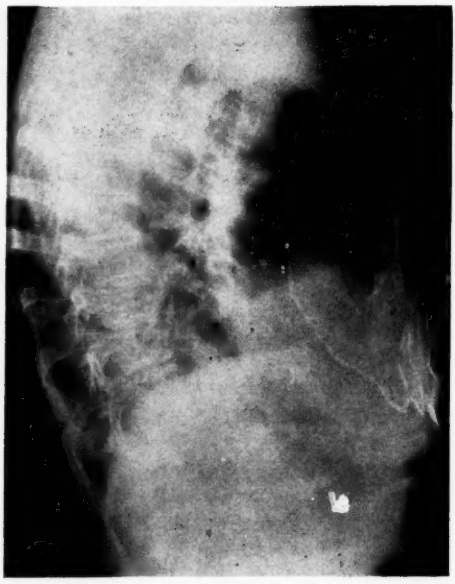
Surgical treatment of chest wall defects has been described in the literature for many years. Methods of correction have been proposed by Maier,[2] Maurer and Blades,[3] Watson and James,[4] and others. Most of these methods are applicable as secondary procedures and involve the use of rib struts, fascial grafts, and dermal transplants. Invariably the authors emphasize the utilization of the patient's own tissues in bridging the defect. Each method has individual merits and disadvantages, and none is adaptable to all situations. In most cases the procedures are applicable as corrective operations after the defects have been established. In addition, the technical aspects are by no means simple, and in some instances considerable caution must be used lest a bad situation be aggravated.

From the Cleveland Clinic and The Frank E. Bunts Educational Institute.
Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

Attempts to bridge defects with foreign substances have been reported by many authors, though generally these adjuncts have been unsuccessful when applied to the chest wall. Plates of silver, steel, plastics, and Vitallium have been utilized in defects of skull and long bones, but they have proved



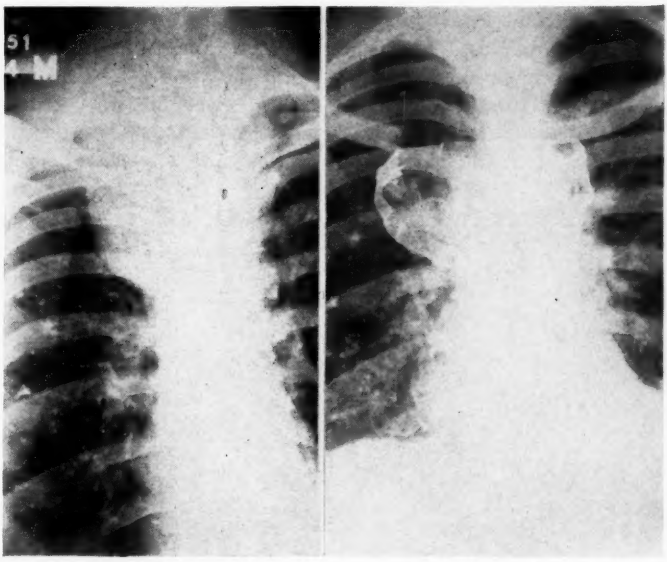
A. *B.*



C.

Fig. 1.—*A*, Primary carcinoma of the breast with invasion and fixation of the underlying chest wall. No distant metastases or lymphatic extension were demonstrated. *B*, Appearance following conventional radical mastectomy with block excision of the anterior chest wall. Tantalum mesh was employed and covered by the thin skin flap. *C*, Radiographic appearance of the thorax after mastectomy and reconstruction with tantalum mesh.

ineffective when used in the chest. In all probability the constant motion associated with the mechanics of respiration, has been the chief factor responsible for the failures when fixed plates are used. It seems unlikely that a plate, regardless of the substance used and its lack of tissue reaction, could become an integral part of the supporting tissues of the chest wall. By its very nature, a smooth plate resists intimacy with surrounding muscle and fibrous tissue; when these structures are subject to constant changes in stress and strain, the possibility of union becomes more remote.



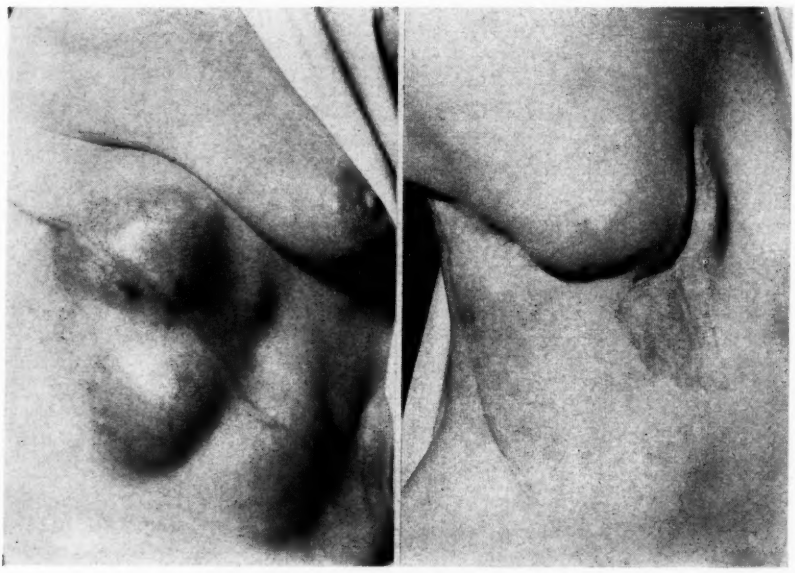
A. *B.*

Fig. 2.—*A*, Roentgenogram demonstrating a large, metastatic, thyroid carcinoma involving the manubrium. A radical thyroidectomy had been performed approximately two years prior to the appearance of this metastasis. *B*, Radiographic appearance of the chest following resection of upper one-half of the sternum and reconstruction with steel mesh. The inner thirds of both clavicles have been removed.

Blades[3, 5] has repeatedly emphasized the hazards in using metal plates to repair traumatic chest wall defects. Griswold[6] and Campbell[7] each report a case where tantalum plates were employed following resections of the manubrium and body of the sternum; in Griswold's case the plate was subsequently removed because of secondary hemorrhages. Campbell expresses the belief that a tantalum plate used for permanent prosthesis would have better chance for success as substitution for the upper half of the sternum than for the lower half. Beardsley[8] used tantalum plates in three cases where large operative defects of the chest wall were created; in each case it was necessary to remove the prosthesis at a later time because of suppuration, presumably due to foreign body reactions. Paulson[9] abandoned the use of tantalum plates on

chest wall defects, attributing failure to the constant motion of the thorax. We are able to find only one report where satisfactory results were obtained and the plate retained its original position.[7]

In 1948, Koontz[10] reported his clinical and experimental results in the use of tantalum mesh to repair ventral hernias. In contrast to a plate, the mesh presents a flimsy screen which is easily cut to desired shape and size. Upon first consideration it does not appear durable nor capable of offering support against mechanical stress, and yet it must be remembered that the principle of the mesh is entirely different from that of the plate. The mesh offers a lattice of nonreactive material which is incorporated rapidly by fibroblasts. The resultant proliferation produces an interwoven, fibrous mass with the lattice acting as the skeleton structure; this differs fundamentally from the encapsulation produced around a flat sheet or cap of metal. As Koontz[10, 11] has shown so conclusively in his experiments, the mesh becomes an integral part of the abdominal wall rather than a tolerated foreign body.



A. *B.*

Fig. 3.—*A*, A large recurrent chondrosarcoma of the chest wall and upper abdominal wall. The incision of the previous operation is clearly visible. Whereas the tumor mass was of considerable size, there was no evidence of distant metastases or extension of the neoplasm through the pleura or peritoneum. The large mass was resected by block excision of the chest wall, diaphragm, and upper abdominal wall; the resected portion of the thoracic cage contained portions of seven ribs. *B*, Appearance of the patient approximately nine months after surgery. Stainless steel employed to reconstruct the chest wall, diaphragm, and upper abdominal wall has given a very satisfactory surgical result. The right breast has been used as a skin flap in an effort to close the original defect; the scar to the right of the midline is that of the releasing incision and skin graft employed at the time of closure.

Mesh prostheses have been employed in twenty-one patients who were operated upon for lesions of the thoracic cage at the Cleveland Clinic. The majority of these patients were treated for primary or metastatic neoplasm of

the chest wall; five patients in this group required corrective surgery for defects produced by trauma or inflammatory disease. In addition to the twenty-one patients mentioned, mesh has been used on five occasions in the treatment of large diaphragmatic hernias and in one instance for the surgical correction of eventration of the diaphragm. Our experience with these patients during the past four and one-half years and our observations are subsequently reported.

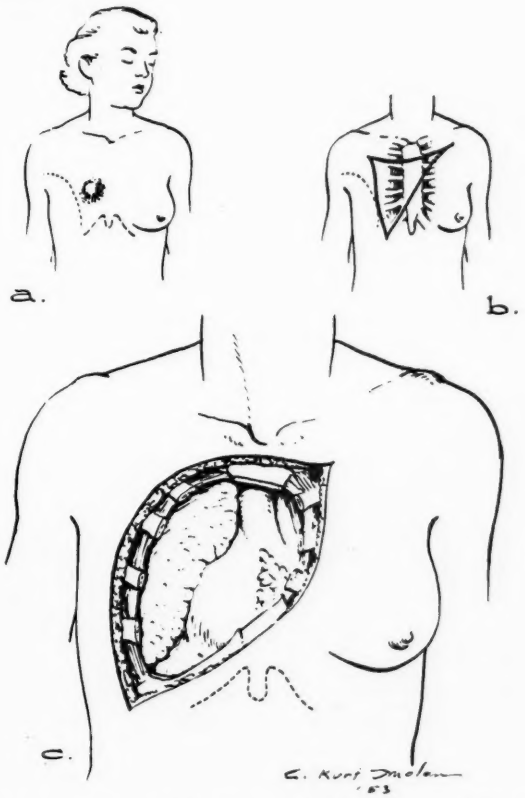


Fig. 4.—This drawing demonstrates the principle of block excision for a malignant neoplasm of the anterior chest wall. *a*, The illustration is taken from a case of recurrent carcinoma of the breast appearing four years after radical mastectomy. *b*, The heavy lines demonstrate the triangular block excised from the anterior chest wall. *c*, The excision includes sternum, ribs, and supporting soft parts. Underlying pleura and mediastinal fascia were included. The pericardium is intact.

TECHNIQUE

Radical excision of the chest wall lesion is carried out under endotracheal anesthesia. Supporting structures of the thorax and upper abdomen are sacrificed without regard for the subsequent closure in order to provide an adequate tissue margin around the neoplasm. Confidence in mesh prostheses has relieved the fear of creating an intolerable defect and thereby improved the caliber of this type of cancer surgery.

Following the block excision and necessary hemostasis, the defect is measured for the mesh prosthesis. The technical aspects of placing mesh are simple. The defect is overlapped by a single or double thickness of mesh which is cut to approximate size; and the edges are turned in to prevent fraying and to provide a more secure border for holding the suture material. Direct contact between mesh and underlying lung, diaphragm, or abdominal viscera may occur without apparent untoward reaction. The prosthesis is simply "tacked in place" with interrupted sutures until it is firmly secured.

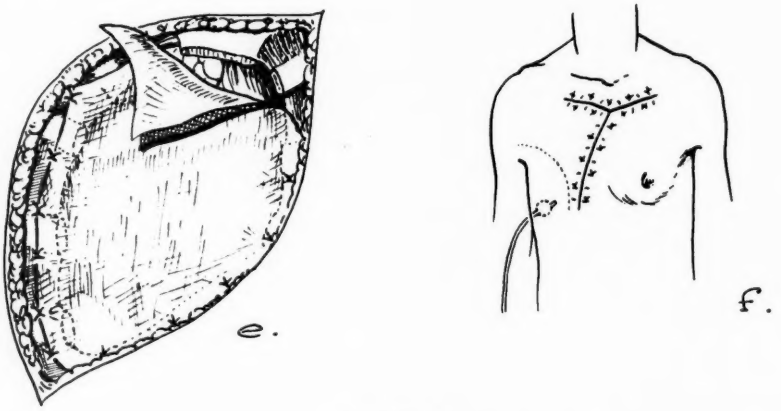
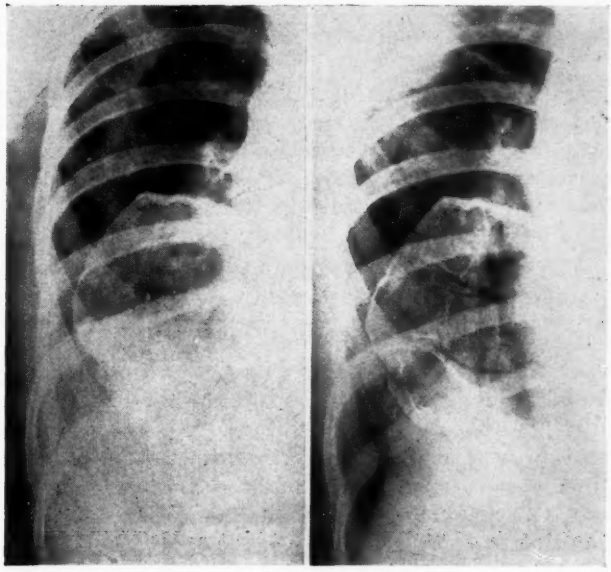


Fig. 4, Cont'd

e, Artist's conception of the mesh as it is employed to reconstruct the chest wall and prevent future parodoxical respiration. A double thickness of steel mesh is "tacked" over the bony thorax with interrupted fine silk sutures. *f*, Diagram of the completed operation showing closure of the skin flaps over the steel mesh. A Foley bag catheter is brought out through a stab wound in the sixth interspace for drainage of the right pleural space.

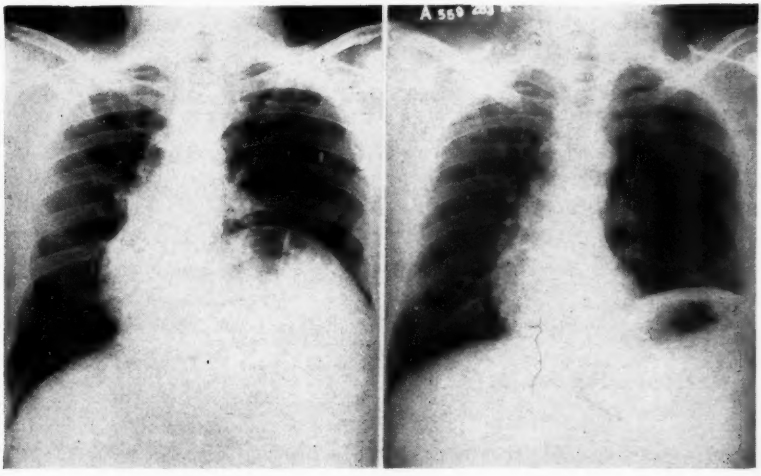
In our early cases, we employed only tantalum sutures for this procedure, fearing an unfavorable tissue reaction if a multiplicity of agents were employed. Experience has shown that this fear is unwarranted, and in the past two and one-half years we have employed fine silk to secure the mesh prosthesis. When the prosthesis is secured, it is covered by skin and subcutaneous tissue. It may be necessary to create large flaps of skin by undermining, and to employ releasing incisions in order to obtain satisfactory closure. In every instance it has been possible to effect primary closure of the wound edges, although grafts to the area of the releasing incision have been necessary. A firm dressing, applied with elastic bandage, need not be excessively bulky nor unduly padded to protect the wound.

In two patients the skin edges suffered necrosis because of excessive tension necessary for closure. The local necrosis produced separation of the wound down to the mesh. Ordinarily such a complication would jeopardize the retention of any foreign body prosthesis, particularly if a plate had been employed; however, in both instances the necrotic areas healed by granulation



A. *B.*

Fig. 5.—*A*, Roentgenogram demonstrating tantalum mesh employed in the reconstruction of the anterior chest wall. This film made about six weeks after operation. *B*, Fourteen months after operation there has been appreciable breakdown of the tantalum mesh. It is my opinion that this is due to fatigability of tantalum mesh and accounts for its inability to tolerate continuous shearing stress.



A. *B.*

Fig. 6.—*A*, Roentgenogram demonstrating eventration of left diaphragm. *B*, Radiographic appearance approximately eighteen months after correction and reinforcement with stainless steel mesh.

and without residual sinus. In no case has it been necessary to remove a part or all of the mesh, nor have draining sinuses attributable to suture material occurred.

Early experience was confined to the use of tantalum mesh.* It proved satisfactory in the immediate postoperative period and the early impression was extremely favorable. However, follow-up studies have repeatedly shown that the tantalum mesh may fracture or disintegrate with the passage of time. For this reason, we changed to stainless steel mesh.† From our experience there seems to be little doubt that stainless steel is superior to tantalum for mesh; it withstands shearing stresses much more satisfactorily, and the factor of fatigability is less apparent.

SUMMARY

Defects of the chest wall secondary to extensive surgical procedures may be prevented by the use of mesh prosthesis which should be applied at the time of the definitive operation.

A series of twenty-one patients, operated upon at the Cleveland Clinic, have been presented; in each patient a mesh prosthesis has been successfully applied. There have been no clinical failures attributable to failure of the patient's tissue to tolerate tantalum or stainless steel mesh.

Mesh prosthesis has also been applied to reinforce reconstruction operations in the diaphragm; six patients were so treated for diaphragmatic hernia or eventration.

Experience in this series of patients suggests that stainless steel mesh is superior to tantalum mesh.

REFERENCES

1. Hedblom, C. A.: Tumors of Bony Chest-Wall; Study of 22 Personal and 78 Collected Cases Since 1921, Ann. Surg. **98**: 528-545, 1933.
2. Maier, H. C.: Surgical Management of Large Defects of Thoracic Wall, Surgery **22**: 169-178, 1947.
3. Maurer, E., and Blades, B.: Hernia of Lung, J. THORACIC SURG. **15**: 77-98, 1946.
4. Watson, W. L., and James, A. G.: Fascia Lata Grafts for Chest Wall Defects, J. THORACIC SURG. **16**: 399-406, 1947.
5. Effler, D. B., and Blades, B. B.: Function of Thoracic Surgery Centers in World War II, Am. J. Surg. **72**: 319-330, 1946.
6. Griswold, R. A.: Osteochondrosarcoma of Sternum; Use of Tantalum Plate as Prosthesis, Arch. Surg. **55**: 681-688, 1947.
7. Campbell, D. A.: Resection of the Sternum for Metastatic Carcinoma, Ann. Surg. **129**: 394-398, 1949.
8. Beardsley, J. M.: Use of Tantalum Plate When Resecting Large Areas of Chest Wall, J. THORACIC SURG. **19**: 444-455, 1950.
9. Paulson, D.: Cited by Maurer and Blades.[3]
10. Koontz, A. R.: Repair of Ventral Hernias With Tantalum Mesh; Preliminary Report, South. M. J. **41**: 214-217, 1948.
11. Koontz, A. R., and Kimberley, R. C.: Tissue Reactions to Tantalum Mesh and Wire, Ann. Surg. **131**: 666-686, 1950.

DISCUSSION

DR. LAWRENCE M. SHEFTS, San Antonio.—The size of the surgical specimens is certainly a compliment to Dr. Effler's surgical ability; the size of the surgical specimen sent to the laboratory was almost as big as the patient. It demonstrates very vividly

*TM 53 gauge, .003 diameter, 50 x 50 mesh—Ethicon
†Surgaloy Product, No. 71, .003 diameter, 50 x 50 mesh—Davis and Geck.

how large defects can be repaired efficiently. I might add that I have had the same experience with the difference in tantalum mesh and stainless steel, and I advise the use of the latter, as did Dr. Effler. The fragmentation he speaks of does not occur in the center of the specimen (having removed one) but it is a tear that starts at the edge and goes right into the specimen; it does not break in the center or in an irregular fashion.

I arise mainly to mention a technique in the use of the mesh that Dr. Effler mentioned. He wants it to become a part of, to become incorporated into the body, and there is a method of using the mesh that will hasten this, particularly when there are some adjacent ribs left to which it can be fastened. In my hurry to leave Texas (not that I was in a hurry to leave, but in my hurried leaving) I left behind the lantern slides that had been prepared, so I call attention to the drawing on the blackboard. This is a cross section of two ribs; the intervening ribs have been removed and all the chest wall, as in one of the cases presented here. The periosteum was then removed from the side near the top edge of each rib, and peeled off the top surface and off the under surface, so that there was a flap of periosteum extending out from these ribs. The mesh was then inserted under the ribs, the ribs above and below the defect drilled, and wire sutures used to attach the mesh to the ribs. Then sutures were used to attach the periosteum as a flap to the wire mesh, so that when bone regeneration occurred it will incorporate itself directly into the wire mesh.

This method is also of value in repair of pulmonary hernias, where the periosteal flaps fail to bridge the space as in the second interspace anteriorly.

I must say again that I enjoyed Dr. Effler's paper very much.

DR. ALEXANDER E. W. ADA, New York.—I would first like to thank Dr. Effler for a most excellent presentation. I have had parallel results in a smaller series of cases and have found this method most satisfactory. In no instance have I observed migration, fragmentation, or extrusion of the mesh or wound infection. A subcutaneous collection of serum has developed at the site of operation. This should be aspirated repeatedly by needle puncture through normal tissue a short distance from the wound.

In 1948 I first employed tantalum mesh to reconstruct the chest wall after surgical extirpation of a tumor. This case and a subsequent one were the basis of a report published in THE JOURNAL OF THORACIC SURGERY (**21**: 125, 1951). I would like to relate briefly the end result in the first case:

(Slide.) This is an anteroposterior x-ray film of the chest showing the tumor presenting itself in the right thorax and (slide) this is a photograph of the surgical specimen.

(Slide.) This is a postoperative x-ray film showing reconstruction of the defect in the chest wall and (slide) another view of the reconstruction.

The tumor was a plasma-cell myeloma which was the only one visible on skeletal x-ray films before operation. The patient succumbed three years later to multiple myelomata in the Memorial Hospital. Dr. Higginbotham retrieved the tantalum mesh at autopsy. The mesh was found to be completely embedded in a thick layer of scar tissue creating a solid chest wall. The pleural surface was smooth and pearl white in color.

(Slide.) This is an x-ray film of a portion of the mesh showing it to be intact with the exception of a portion at the right, which was damaged in its removal.

(Slide.) I am indebted to a most industrious resident for this slide. It is a photomicrograph of a section taken through the tantalum mesh and scar tissue. Three wires are visible, embedded in a homogeneous fibrous tissue with minimal round cell reaction which is represented by a few giant cells.

DR. HARVEY J. MENDELSOHN, Cleveland.—I wish to compliment Dr. Effler on this excellent series of cases, and I wish to mention my limited experience in three operative cases involving two patients.

One, which I will mention briefly, was merely the replacement of a defect following lobectomy in a patient who had had a shell fragment wound. This was a simple case;

following right lower lobectomy, the replacement of the defect which had been previously present solved the difficult closure problem and the patient had an uneventful recovery with no difficulty in re-expansion.

The next patient was a young man who had had a fibrosarcoma of the chest wall locally excised previously; only one rib was removed. Within one year he had a recurrence, and the first slide shows this in the chest wall at this point. Within a few months it had grown to this size involving the left lung. The lesion was excised by a large en bloc excision, removing the fourth, fifth, sixth, and seventh ribs from the anterior to the posterior axillary line. Dr. Effler mentioned and Dr. Ada showed the problem of preventing paradox. It was thought best to prevent paradoxical motion with a wide sheet of 6 by 12 inch tantalum supported by a rib strut. This was done by bisecting the eighth rib longitudinally, preserving its periosteum, fracturing it posteriorly at its neck, and measuring it so that it coincided with the anterior limit of the excision at the fourth rib.

The interesting part of this is, unfortunately for the patient, that within a year he again had a recurrence of this fibrosarcoma in the lung, and on doing a pneumonectomy we obtained this specimen which includes the tantalum mesh chest wall, rib strut, left lung, and a portion of the left diaphragm.

(Slide.) Here it is possible to see the outer surface of the specimen. I had resected a portion of the scapula in the previous operation so as to prevent a serous pocket from forming and there was no such pocket. The muscle had grown into the tantalum mesh, which had also fragmented. I do not have slides of the sections here, but there was muscle growing into the tantalum mesh with practically no reaction at the site of the tantalum.

(Slide.) This shows the lung and a portion of the diaphragm removed with the tumor. The diaphragm here and the bronchus here, and there is some recurrent tumor in this area.

I present this case chiefly to show two things: a method of preventing as much as possible paradox by using a rib strut beneath the mesh, and also the fact that with tantalum mesh (or subsequently I have used stainless steel mesh) there is practically no reaction. Following pneumonectomy this patient had very little trouble. There was little or no paradox, and he had an uneventful recovery from the operation. Ultimate prognosis, however, is poor.

DR. BERT H. COTTON, Los Angeles.—I rise for three reasons: First, to say how much I enjoyed Dr. Effler's excellent paper. Second, to concur with his encouraging observations by reporting fourteen cases with favorable results in block resection of the chest wall and prosthesis by stainless steel wire mesh. Third, to present one case which I thought might be of interest:

(Slide.) This illustrates a case of block resection of a chest wall and pectoralis minor muscle for sarcoma, the attempted prosthesis, and the result. Here is seen the tumor involving the upper half of the right chest wall.

(Slide.) The resected block of chest wall including the second, third, fourth, fifth, and sixth ribs, from the transverse processes to the sternum, and the lateral half of the seventh rib is shown here.

(Slide.) This x-ray film shows an 18 inch sheet of heavy screen wire, No. 40 stainless steel mesh, molded to the contour of the right hemothorax.

(Slide.) Here is a back view of the patient; the scapula has caused buckling of the posterior portion of the prosthesis; the mesh we felt was not heavy enough.

(Slide.) The front view shows a satisfactory cosmetic result. There is slight prominence of the right pectoralis area due to the posterior buckling of the prosthesis.

Again, may I offer congratulations to Dr. Effler.

DR. EFFLER (Closing).—I am grateful to the discussants of this paper and in particular would like to thank Dr. Shefts for his kind remarks. The method of applying a mesh which he has described is a definite refinement, and I am sure is an improvement over that presented today. I would like Dr. Shefts to know that all the surgical specimens were not of the magnitude shown on the screen; knowing that some Texans would be present I brought only the largest.

If my memory is correct, Dr. Ada was one of the first to report on the use of tantalum mesh and reconstruction of the chest wall. I gathered from his remarks that he has not been impressed with fragmentation of tantalum mesh; certainly this has been the rule rather than the exception in my series. However, I believe it will be more apparent on the anterior chest wall than posteriorly. Someone, I believe Dr. Babcock of Philadelphia, has tested the shearing strength of various types of inert materials on a mechanical device and has demonstrated that stainless steel will tolerate this type of activity much better than tantalum.

Dr. Mendelsohn calls attention to the frequency of recurrence of fibrosarcomas in the chest wall. Many of the cases in this series were recurrent tumors, which emphasizes the necessity of an extensive well-conceived operation that is correctly performed the first time. Experience encourages me to believe that there is almost no limit to the amount of chest wall that can be removed if a mesh prosthesis and an adequate skin closure can be employed. The type of operation that is inadequate in its basic conception will only be rewarded with recurrent neoplasm of the chest wall and necessitate multiple procedures with a correspondingly poor prognosis.

I appreciate very much the opportunity of appearing before this Association; again I would like to thank the discussers of this paper.

AN OPERATION FOR CHRONIC PLEURAL EMPYEMA

FREDERICK G. KERGIN, M.D., M.S., F.R.C.S.
TORONTO, ONT.

A PLEURAL empyema can be termed chronic only when, in spite of adequate drainage, the pleural space shows no appreciable tendency to decrease in size. The ideal solution for this situation is to obliterate the space by causing the lung to expand by the use of some form of decortication. However, there remains a group of patients to whom this ideal treatment cannot be applied. Occasionally decortication is technically impossible; more often the lung cannot, or should not, be expanded because of an intrinsic disease, and sometimes the lung has been removed previously. For these patients the surgeon must resort to thoracoplasty. If the process is truly chronic there is invariably deposition of fibrous tissue on the parietal pleura. This tissue may be sufficiently rigid so that even after removal of the ribs the chest wall cannot fall in to conform to the shape of the cavity and so lead to the healing of one surface to the other to produce obliteration of the space.

The operation described by Schede in 1890 was founded on an accurate knowledge of the pathology of chronic empyema and was a great step forward, but it has serious faults; it is shocking and mutilating, it sacrifices intercostal nerves with resulting cutaneous anesthesia and paresis of the abdominal wall, it leaves a large open wound requiring a long period of packing and dressing before healing is complete, and it leaves an unstable chest wall. After healing occurs, the rigid visceral layer of fibrous tissue lying on lung and mediastinum becomes thinner so that instability develops; paradoxical movement is a problem and the heart is unprotected. Various modifications of the operation have corrected some of the faults. The modifications of Roberts leave a stable chest wall but sacrifice the nerves, and the wound is packed open, which leads to slow healing. Heller, in 1934, described an operation in which, after removing the ribs overlying the cavity, the rib beds are incised to create a series of ribbons; each of these ribbons consists of an intercostal muscle with the accompanying vessels, nerve, underlying parietal pleura, and fibrous tissue. These ribbons are dropped into the cavity to act as space-fillers. In 1935, Wangensteen described the same procedure with certain modifications designed to make the ribbons more mobile, and so more adaptable to the shape of the cavity.

The Heller-Wangensteen operation is effective and overcomes all the serious faults of the Schede procedure: the intercostal nerves are preserved; the periosteum remains, allowing rib regeneration to provide a stable chest wall; and the wound can be closed with tube drainage. Some fifteen years ago Dr. N. S. Shenstone, Dr. R. M. Janes, and I modified the operation still

From the Department of Surgery, Faculty of Medicine, University of Toronto, and the Surgical Service of the Toronto General Hospital.
Received for publication March 9, 1953.

further to overcome one remaining difficulty. It was found that even with the maneuver suggested by Wangensteen the ribbons were somewhat rigid and not long enough to adapt themselves easily to all corners of the empyema cavity; by excising the parietal pleura with its thick layer of fibrous tissue this difficulty was overcome, and the added advantage was gained of filling the space with muscle tissue, well supplied with blood, which rapidly threw out granulations to become adherent to the visceral layer. Since that time this operation has been used on many occasions for chronic cavities, both pleural and extrapleural in situation, and has proved extremely satisfactory. Only very recently have we learned that Grow gave an excellent description of the same procedure in 1946. However, judging by recent publications on the treatment of epyema and also from discussions with thoracic surgeons, it appears that this operation is little known and seldom practiced; Sweet in a recent textbook of thoracic surgery describes only the original Schede operation. It seems worth while to describe the operation again, indicating its advantages and limitations, in the hope that it will become more widely used.

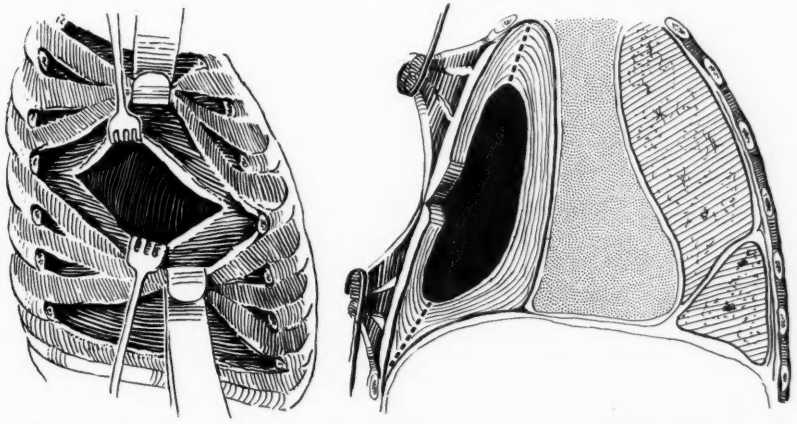


Fig. 1.—The diagrams illustrate the treatment of a chronic empyema following pneumonectomy. Guided by inspection of the open empyema cavity, all the ribs overlying the space have been resected and the intercostal muscle bundles freed. The parietal wall will be resected as indicated by the dotted lines.

THE METHOD

An incision is made which permits exposure of all the ribs overlying the cavity and three or four of the ribs over the center of the space are resected. The periosteum of each rib bed is then incised in a linear fashion, and by a combination of sharp and blunt dissection in the plane of the endothoracic fascia the intercostal muscle bundles between the resected ribs are freed intact and retracted out of the way. In the space so cleared the parietal pleura is widely incised and the interior of the cavity inspected. With the open cavity as a guide, it is then possible to resect all the ribs overlying it, in each case carrying the resection about one inch beyond the limits of the space. The corresponding

intercostal bundles are then freed throughout their length, to result in the situation illustrated in Fig. 1. The bundles were shortened by the contraction of the fibrothorax; when liberated they lengthen and become quite slack, so are easily retracted, and later will fall into the cavity without tension. The parietal wall of the cavity is completely excised, taking care to bevel the edges in order to prevent kinking of the bundles and overhang of the edges of the cavity. The intercostal muscle bundles, of ample length, are simply laid in the cavity in parallel rows, as shown in Fig. 2, a tube laid over them, and the superficial muscles and skin sutured. It is of some advantage to institute closed drainage and after the first few hours to apply suction. Healing has been invariably by first intention; the tube can be removed in five to seven days.

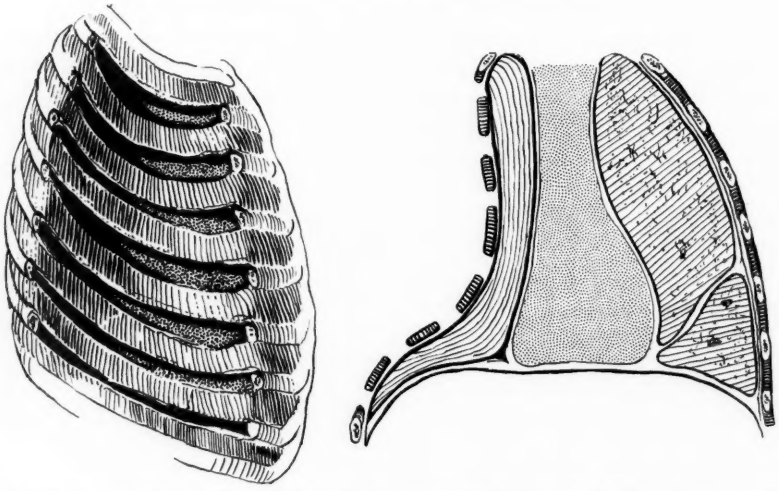


Fig. 2.—After resection of the parietal wall the muscle bundles are laid in the cavity. A tube is placed outside the bundles and the superficial muscles and skin sutured.

Because the mediastinum is protected by a rigid layer of fibrous tissue this operation produces no marked physiologic upset, the chief problem being loss of blood. If this is replaced in a quantitative manner, even very extensive thoracoplasty operations may be completed in one stage.

A bronchial fistula, if present, must be dealt with as seems most appropriate; occasionally the bronchus can be dissected free and sutured with an intercostal muscle to reinforce the suture line, more often the edges are simply freshened and an intercostal muscle sewn over or into the opening. In either case it is wise to lead a tube down to the neighborhood of the fistula and leave it there until there is good evidence that the fistula has healed; otherwise coughing may blow out air to create a small pocket around the opening of the fistula and this may persist.

DISCUSSION

The advantages of this method are that it is usually a one-stage procedure, the intercostal nerves are preserved, the ribs regenerate to give a stable chest

wall, the space is filled with living tissue with excellent blood supply which rapidly throws out granulations to become adherent to the visceral wall, fistulas may be dealt with directly, and the wound is sutured and heals by primary union. The mobilized intercostal muscle bundles are of ample length and completely pliable so that they adapt themselves perfectly to the shape of the visceral layer leaving no unoccupied corners.

With certain modifications, mentioned below, the operation can be used for any chronic pleural or extrapleural cavity, provided there has not been a previous unsuccessful extrapleural thoracoplasty. In such a case it is not possible to resect the reformed ribs without damaging the intercostal muscle bundles. We have applied the operation to chronic nontuberculous empyema, to empyema following lobectomy or pneumonectomy, to tuberculous empyema with and without secondary infection, and we have used it to close cavities remaining after extrapleural pneumothorax or plombage therapy. Many of the tuberculous cases were operated upon before streptomycin was available but in only one patient, to be mentioned later, was there a tuberculous wound infection.

There has been no death attributable to this operation and only two complications. One patient had a reactionary hemorrhage on the night of operation which required reopening the wound and packing; this delayed healing but the result was otherwise satisfactory. The other complication emphasizes the one contraindication to this type of operation. One of our patients had an apical tuberculous empyema as the result of pneumothorax therapy and there was a small bronchial fistula; after treatment, as described previously, he developed a tuberculous subscapular infection which required treatment by a pedicle muscle graft for which pectoralis major was used. For a tuberculous empyema lying under the scapula the operation should be modified.

If the tuberculous empyema is complete, an upper seven-rib extrapleural thoracoplasty is done as a first stage. About four weeks later the lower part of the cavity is dealt with through a fresh incision, the intercostal muscles being freed as usual and the parietal wall excised. If, as is usually the case, the previous extrapleural thoracoplasty has failed to obliterate the upper part of the cavity and there is a narrow tunnel left posteriorly, one or two intercostal muscles may be divided anteriorly and tucked into this space as a muscle graft, and the operation on the lower chest completed in the usual fashion. This combined procedure is very effective, and, since the subscapular space is not opened at the second operation, there is no danger of infecting it.

To obtain collapse of a very thick-walled apical extrapleural space complicated by tuberculous infection, the result of extrapleural pneumothorax therapy, a different modification has been used on one occasion, with success. After resecting the overlying ribs and mobilizing the muscles as usual, the thick parietal wall was shaved down with a scalpel until it became thin and pliable, but care was taken not to enter the cavity. Aspiration of the contents then caused the parietal wall to collapse against the visceral surface, the bundles were laid on top and the wound closed.

By modifications such as these, this method of thoracoplasty can be adapted to the treatment of any chronic empyema, provided the chest wall has not been mutilated by a previous thoracoplasty operation.

SUMMARY

1. The principles involved in the treatment of chronic empyema are discussed.

2. The disadvantages of the Schede operation and certain modifications of it are stated.

3. An operation, which is essentially the same procedure as that published by Grow, is described, with certain modifications which may be necessary for special problems. It has proved very satisfactory over a period of fifteen years in the treatment of all varieties of nontuberculous and tuberculous chronic empyema.

REFERENCES

1. Schede, M.: Die Behandlung der Empyeme, Verhandl. d. Cong. f. innere Med., Wiesb. **9**: 41, 1890.
2. Roberts, J. E. H.: The Lettsomian Lectures, Tr. M. Soc. London **58**: 204, 1935.
3. Heller, H.: Ueber Verhutung und Behandlung der Empyemresthohlen, Chirurg. **6**: 297, 1934.
4. Wangensteen, O. H.: The Pedicled Muscle Flap in the Closure of Persistent Bronchopleural Fistula, J. THORACIC SURG. **5**: 27, 1935.
5. Grow, J. B.: Chronic Pleural Empyema, Dis. Chest **12**: 26, 1946.
6. Sweet, R. H.: Thoracic Surgery, Philadelphia, 1950, W. B. Saunders Company, p. 108.

EMERGENCY PULMONARY RESECTION FOR MASSIVE HEMOPTYSIS IN TUBERCULOSIS

C. A. Ross, M.D.
Edmonton, Alberta

ONE of the most alarming complications of pulmonary tuberculosis is massive hemoptysis. Such an occurrence terrifies the patient and distresses the physician.

Approximately one-third of patients with pulmonary tuberculosis will have hemoptysis but this reaches alarming proportions in only about 2 per cent of the cases.

Such gross hemorrhage is a dangerous complication of tuberculosis. The patient, who does not succumb to exsanguination or to suffocation by aspirated blood, very frequently develops a diffuse bronchiogenic spread of the disease which may cause death at a later date.

SOURCE OF HEMORRHAGE

It is recognized that major hemorrhages are usually associated with the chronic fibrocavernous type of phthisis. The bleeding is due to the rupture of a small aneurysm in the wall of a cavity in most instances. These aneurysms were first described by Fearn[1] in 1841, but Rasmussen of Denmark[2] did extensive work on this subject and the lesions have been named "Rasmussen Aneurysms." Most investigators have concluded that the vessels involved are branches of the pulmonary arteries but more recently Cudowicz[3] has shown by an excellent series of investigations that the blood supply to the lung in these areas of fibrotic tuberculosis is mainly by way of dilated bronchial vessels and that these aneurysms are probably of bronchial rather than of pulmonary arterial origin.

METHODS OF TREATMENT

The usual methods used to control hemoptysis include: rest, sedation to calm the patient and to prevent excessive coughing, vitamin K and systemic coagulants. Some believe that ice bags applied to the chest may be of some value. Artificial pneumothorax, induced on the affected side, when possible, may be useful. Phrenic crush, pneumoperitoneum, emergency thoracoplasty and emergency plombage have all been employed for the control of hemorrhage from tuberculous disease.

Although gastric resection, in certain cases of massive bleeding of gastric origin, is an accepted procedure, the concept has not generally been extended to uncontrollable pulmonary hemorrhage, associated with tuberculous disease. A review of the pertinent literature reveals only one such case report,[4] although it is most likely that there are unreported cases in which the operation has been performed.

From the Aberhart Memorial Sanatorium.
Received for publication March 4, 1953.

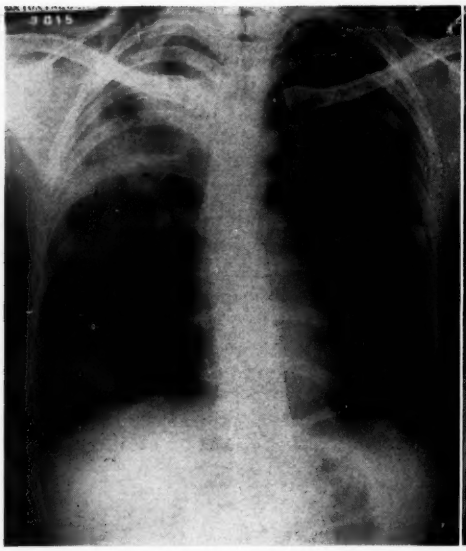


Fig. 1.

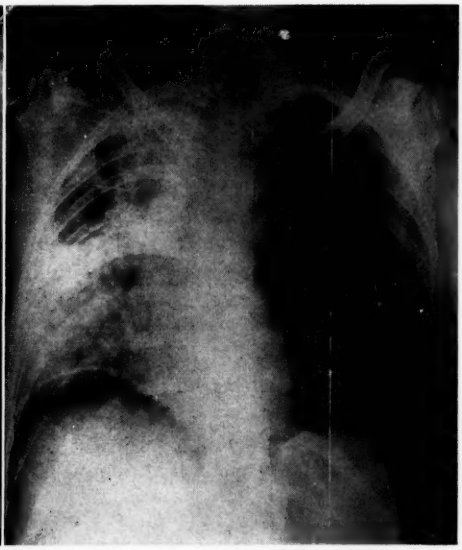


Fig. 2.

Fig. 1.—Admission x-ray photograph, April, 1951, appearance remained essentially unchanged until hemoptysis one year later.

Fig. 2.—X-ray film taken after first hemoptysis, showing diffuse bronchiogenic spread to the right lower lobe. Pneumoperitoneum has been partially removed because of dyspnea.

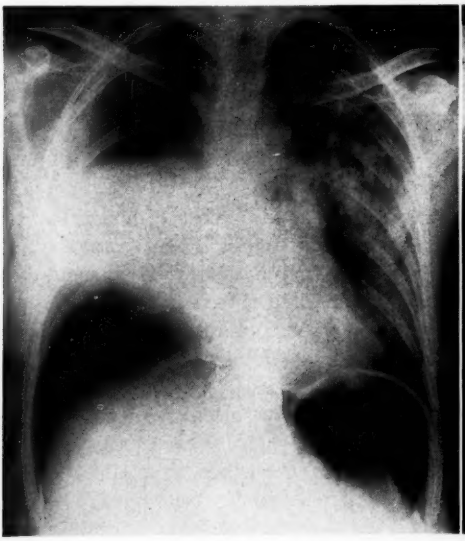


Fig. 3.

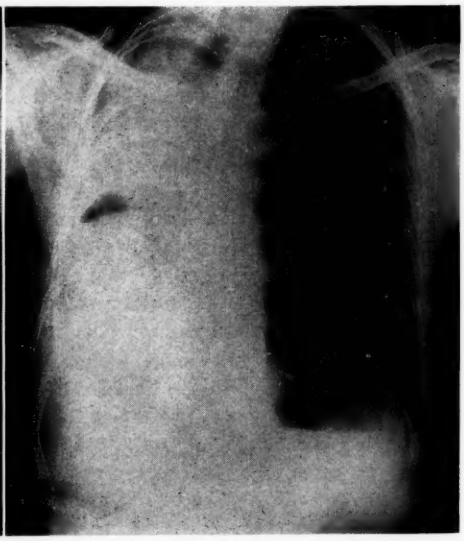


Fig. 4.

Fig. 3.—Roentgenogram showing postoperative contralateral spread of disease.
Fig. 4.—Predischarge x-ray picture showing patient's present status.

It is recognized that pulmonary resection to control hemorrhage due to trauma is not an unusual occurrence. Such a procedure falls into an entirely different category from the case under discussion.

The following report is presented in an attempt to stimulate further interest in this procedure as a lifesaving measure in certain instances of hemorrhage from pulmonary tuberculosis.

CASE REPORT

Mrs. M. R., aged 45, was a woman of French and North American Indian extraction. She was admitted for treatment of pulmonary tuberculosis in April, 1951. At that time she had moderately-advanced disease involving the right lung. The x-ray pictures showed that the upper lobe was fibrotic and contained a large cavity while the lower lobe showed scattered nodulation and fibrosis. The sputum was positive for tubercle bacilli.

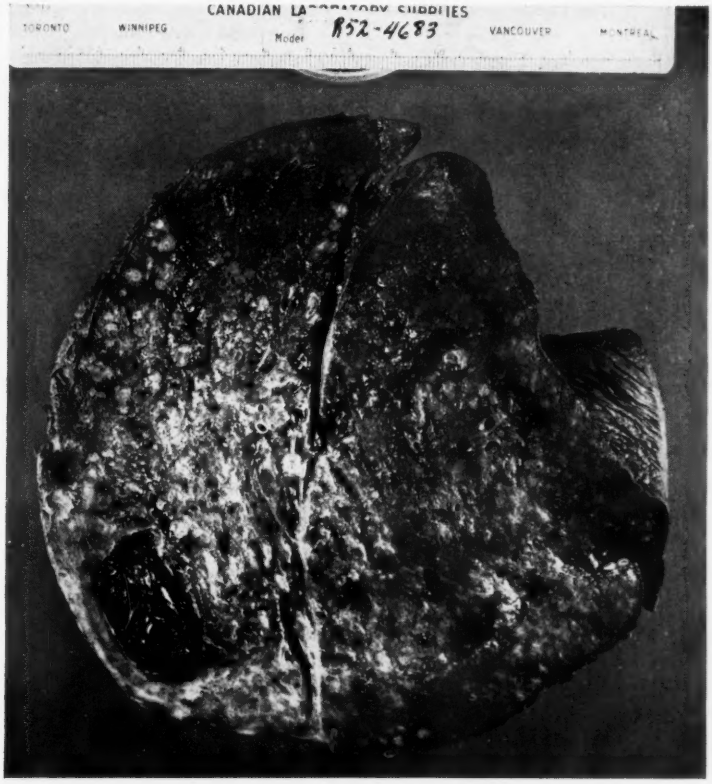


Fig. 5.—Resected specimen. Right lung. Note large upper lobe cavity filled with blood clot and diffuse bronchiogenic spread of disease.

She had had more than her share of tribulations. Past history included the loss of one eye in an accident; an appendectomy; severe burns of the face, trunk, and arms; and a cholecystostomy followed by a cholecystectomy which left a "postcholecystectomy syndrome." She also had an untreated congenital dislocation of the left hip.

Although it was obvious that "conservative" methods of treatment would be of no value in this case, a pneumoperitoneum was induced in an attempt to improve the patient's condition. Resection was considered, but postponed because the patient was not considered to be a fit subject for surgery at that time: Hemoglobin was 62 per cent of normal; albumin-globulin ratio was reversed; the cephalin flocculation was two plus. She also had considerable gastrointestinal disturbance which was only partially controlled by diet and antispasmodics.

On May 21, 1952, after a rather large pneumoperitoneum refill, she began to cough up some bright red blood. The hemorrhage soon became profuse and during the following four days she had repeated large hemoptyses varying in amount from 10 to 20 ounces of blood at a time. By May 25 the bleeding had almost ceased. Hemoglobin determination at this time was 51 per cent of normal. A blood transfusion (500 c.c.) was given.

X-ray films at that time showed a diffuse spread of the disease to the lower lobe of the right lung, and the temperature was elevated to 103° F.

On May 29, she began to have further profuse hemoptyses. This continued during the day and by early evening she was in extreme shock and it was not possible to determine the blood pressure. Further transfusion was started but replacement did not keep pace with the continued loss of blood. A second transfusion was started in another limb and with both running under pressure, she was taken to the operating room for an emergency pneumonectomy.

After induction of the anesthesia, she was bronchoscoped and considerable blood was aspirated from the trachea and bronchi. A Thompson bronchus block was introduced into the right main-stem bronchus and the balloon inflated. This controlled further flooding of the opposite lung with blood. With the patient in the lateral position, a right thoracotomy was done and a rapid pneumonectomy performed. Mobilization of the lung, done extrapleurally, was difficult because of extremely dense adhesions. During this procedure the azygos vein was inadvertently torn causing troublesome hemorrhage. The bronchus was closed with a single row of interrupted vertical mattress sutures.

Postoperatively the patient's condition was only fair. Blood pressure remained at approximately 70 to 80 mm. mercury, systolic for twenty-four hours, in spite of what is usually considered to be adequate blood transfusion. She had in all 8,000 c.c. of blood, including the two bottles which were running at the time she was taken to the operating room.

Temperature, which had been 104° F. immediately prior to the operation, dropped to normal the next day and remained so until the sixth postoperative day when it again rose to 101° F. and a definite contralateral spread of the disease was noted.

Dihydrostreptomycin (1 Gm. daily) was started on May 22, after the first hemoptysis. Following the operation 1 Gm. twice daily was given. This was continued until July 4, when it was changed to 1 Gm. three times weekly and so continued until October 7. Streptomycin had to be discontinued at this time because of complaints of nausea which seemed to be associated with the use of the drug. PAS, 12 Gm. daily, was given in conjunction with the streptomycin from May 30, onward. Isonicotinic acid hydrazine, 200 mg. daily, was commenced on June 19, and has been continued until the present writing. PAS solution containing 10 Gm. of the drug was introduced into the right pleural space every other day for two weeks postoperatively.

A small pneumoperitoneum was maintained until November 1, to help reduce the size of the right hemithoracic space.

The patient was discharged from the Sanatorium on Jan. 13, 1953. At present she is well, steadily gaining weight and x-ray pictures show no evidence of active disease in the contralateral lung. Examination of sputum and fasting gastric juice on repeated occasions have not shown the presence of tubercle bacilli on either smear, culture, or guinea pig inoculation.

DISCUSSION

It is interesting to note that even though the operation was performed in the face of an acute exacerbation of the tuberculous process, and on a patient who was a very poor surgical risk, the outcome was gratifying. It is also noteworthy that a contralateral spread of the disease appears to be controlled by prolonged antibiotic therapy.

Technical considerations of importance are: (1) Excellent anesthesia is most necessary. (2) Large amounts of blood transfusion must be given, particularly during the operation. (3) Endobronchial tamponade prior to beginning surgery is the ideal method of positively controlling the hazard of aspiration of blood by the other lung. (4) Although speed in surgery is not generally important with the advantages of present-day anesthesia and blood replacement therapy, this is an instance when speed is necessary. Such a patient cannot stand prolonged operative procedure. (5) Prolonged antibiotic therapy is necessary in addition to surgery.

It is difficult to list indications for surgical intervention in these cases but it is obviously unwise to attempt the procedure unless the contralateral lung is either free of disease or has only minimal disease present, and that should preferably be in a stable state. Conservative measures should first be tried to control the situation, but surgery should not be delayed until a massive contralateral spread of disease has occurred or the patient is in such poor condition as to be beyond surgical help.

Usually the simpler operation of pneumonectomy will be preferred to lobectomy but in certain instances the latter may be indicated.

SUMMARY

A successful emergency pneumonectomy for massive hemoptysis complicating pulmonary tuberculosis has been presented.

Some suggestions have been made regarding the treatment of these cases.

I would like to thank Dr. Nelson Nix of Edmonton who very ably handled the difficult anesthetic problem that this case presented, and the Medical Staff of the Aberhart Memorial Sanatorium for their assistance and cooperation.

REFERENCES

1. Fearn, G. W.: Aneurism of the Pulmonary Artery, Lancet **1**: 697, 1840-1841.
2. Rasmussen, V.: On Hemoptysis, Especially When Fatal, in Its Anatomical and Clinical Aspects, Edinburgh M. J. **14**: 385, 486, 1868.
3. Cudowicz, Leon: Blood Supply of the Tuberculous Lung, Thorax **7**: 270-276, 1952.
4. Ryan, Thomas C., and Lineberry, William T., Jr.: Pneumonectomy for Pulmonary Haemorrhage in Tuberculosis, Am. Rev. Tuberc. **61**: 426-430, 1950.

Announcement

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The 34th annual meeting of the American Association for Thoracic Surgery will be held May 3, 4, and 5, 1954, in Montreal, Que., Canada. Headquarters will be at the Sheraton-Mount Royal Hotel.

Requests for Hotel Reservations

These should be mailed *directly* to the Reservation Manager, Sheraton-Mount Royal Hotel, Montreal, Que., Canada. Please mention this Association, type of accommodation desired, date, and approximate hour of arrival. If accommodations are desired elsewhere, please communicate directly with hotel of your choice.

Thoracic Surgical Forum

After due consideration, the Council has decided to try an experiment by assigning one morning session to a "Thoracic Surgical Forum" for the presentation of short papers on current thoracic research, anatomy, modified surgical techniques, etc. Papers at this session will be limited sharply to ten minutes (including the showing of lantern slides or other illustrative material) with three minutes as the maximum discussion of each paper.

These papers will be published together in one issue of THE JOURNAL OF THORACIC SURGERY. Maximum length: 3,000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts for Papers

Abstracts for the presentation of papers at the 1954 meeting, including papers before the Forum, must be received on or before January 1, 1954, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Forum" or "For Regular Program."

Five, repeat five, copies of each abstract should be sent to the Secretary of the Association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Jan. 1, 1954, to be considered for action in Montreal. Applications received beyond this deadline will be deferred for consideration until 1955.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the sponsoring statement on the application form, the sponsors *must* submit a separate letter concerning the applicant direct to Dr. Lyman H. Brewer, III, Chairman of the Membership Committee, 2010 Wilshire Blvd., Los Angeles, Calif. Completed application forms should likewise be sent to Dr. Brewer. These regulations are at the direction of the Council and were made effective in 1952 at Dallas.